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The Significance Of Abnormal Metabolic Features In The Management Of Thyrotoxicosis*

WALTER B. PALMER, *New York*

THE management of the thyrotoxicoses is a popular topic for medical meetings and medical journals. During the past few years scores of articles dealing with this phase of the thyroid problem have appeared. Generally the authors are on the defensive, advocating either surgical or medical treatment. At the outset I wish to make it clear that this is not my intention. Many clinicians prefer to postpone surgery until all medical measures have proved of no avail. In some of the hospitals a case of exophthalmic goiter is seldom if ever seen on the medical services, while in others the medical and surgical men work together. At the Presbyterian Hospital, in New York, we have a combined medical and surgical thyroid clinic. All cases with toxic symptoms enter the medical service and the combined group decide as to the course considered best for the individual case. While not all cases are treated surgically, the majority having moderately severe or severe symptoms, provided there is no contraindication, are advised to take the operative course and are prepared for operation on the medical service.

The medical and surgical men meet together in the dispensary for follow-up work, consultations and treatment of the non-operative cases. After several years' experience in the combined clinic certain abnormal metabolic features in the condition appear to need more consideration than they seem to receive generally to the cure of the thyrotoxic, no matter whether surgical or medical.

Since the earliest description of Exophthalmic Goiter by Parry, Graves and Basedow, clinicians have been impressed by the marked loss of weight, weakness and frequent occurrence of troublesome diarrhea. Gradually there have accumulated numerous observations made in the laboratory—nitrogen loss; the difficulty of maintaining nitrogen equilibrium even with high caloric diets; elevated basal metabolism; an upset creatin-creatinin mechanism; inability to store glycogen with the associated alimentary glycosuria, transitory spontaneous glycosuria and occasional development of diabetes mellitus; disturbed fat metabolism reflected in the high cholesterin and fat contents of the blood; loss of phosphorus and calcium related in all probability to the diminished density of the bones as revealed by X-ray; which indicate a widespread disturbance of

*Presented at the Boston Meeting of the American College of Physicians, April 11, 1929.

metabolism. The significance of some of these facts is not clear. In the case of others we find valuable aids in the management of the thyrotoxicoses.

Probably the most widely employed and useful laboratory aid is the determination of the basal metabolic rate. Certainly most will agree that in a majority of instances the degree of elevation is an indication of the severity of disease process and serves as a guide in any particular method of treatment.

On the other hand we encounter cases where we must rely on good clinical judgment rather than depend entirely on the results of the basal metabolic determination. Two cases may be presented to illustrate this point.

A school teacher, thirty-seven years old, having enjoyed good health up to a few months before coming under observation, became weak, nervous, irritable, losing weight in spite of a good appetite, develops exophthalmos, a symmetrically enlarged thyroid gland, tachycardia and tremor. She did not benefit by her summer vacation and was unable to take up her teaching in the autumn. Her basal metabolic rate was +35. Pulse 100-110. The general appearance was one to suggest a severe Graves' and predict a long protracted course as the result of medical care. She was much opposed to surgical interference so that rest in bed for one month combined with radiotherapy for four months was tried out without benefit. As the result of this disappointing trial she consented to a partial thyroidectomy which was carried out with marked immediate improvement. After four months' rest she resumed her usual teaching schedule without difficulty and has remained at her work for a year and a half.

Contrast this case with the second, a laboratory technician of 30, who began to lose weight, became nervous, weak, tiring easily, sleepless, complaining of palpitation, during a period of four months before seen. She was a small, thin girl with no exophthalmos, only a slightly enlarged gland, marked tremor, hot moist skin, pulse rate of 100-110, and a basal rate of +40. After two months' rest she was markedly improved, gained in weight, pulse 80-88, a slight tremor and the basal rate had come down to +20. She resumed work in the laboratory where she has been for nearly a year. She has from time to time taken a little Lugol's solution. It is true she may have a remission more serious than the initial attack.

The two cases were alike in several respects. The basal metabolic rates were approximately the same, +35 and +40, the pulse rates the same, duration of the symptoms the same, yet the disease clinically seemed more severe in the first case than the second. Nervousness and weakness were more marked, the first girl could not carry on and the second could. It was not the basal metabolic rate which determined the course followed in treatment but the clinical condition.

Cases could be multiplied demonstrating the discrepancy between the clinical condition and the elevation of basal metabolism. There are those with a high basal who carry on their daily activities without difficulty and

apparent damage to their circulatory system, others who with a normal basal are invalids and develop cardiac failure. Illustrations are to be found in all groups no matter the type of treatment. I have been impressed with the occurrence of very high basal rates (+60 to +80) in some of the cases of secondary Graves' (toxic adenoma) with only mild toxic symptoms clinically. These cases usually withstand operations well while in some of the younger primary Graves' cases with basal rates between +40 and +50 the toxic manifestations clinically are severe and frequently cause much concern and worry post operatively.

The value of iodine in preparation for operation is now too well known to need comment. The reduction of the basal together with amelioration of symptoms is most striking after the administration of small amounts of iodine. The optimum effect usually occurs in from one to three weeks. Smith has observed that patients not under the full effect of iodine have a more labile basal metabolic rate than those where the effect is optimum. News of the impending operation causes the basal metabolic rate to rise markedly in the first instance while if the iodine has produced its maximum effect the basal is unchanged when surgical measures are discussed. It is suggested that this procedure may be employed to determine whether the optimum effect of iodine has been reached. Such a procedure is time consuming but may be serviceable in doubtful cases.

The difficulty in establishing nitrogen equilibrium, first observed by Frederick Müller, is, I believe, of considerable importance in the dietary control of patients with thyrotoxicosis. A great deal has been said about the use of a high caloric diet but too frequently not sufficient attention is devoted to its accomplishment. In connection with studies to be mentioned later I have had occasion to follow the nitrogen balance in several of our cases. It was found, as Sturgis[1] points out, that in the more toxic cases a caloric intake of 75%, to 100%, above the actually determined basal with the patient in bed, was necessary to establish nitrogen equilibrium or a positive balance. In a few instances more than 100% was required. In others, however, 50% above the basal was sufficient to maintain nitrogen equilibrium and a constant or slight gain in weight. There is a variation among patients in this respects which is difficult to explain. It does not necessarily hold that the higher the basal the larger the percentage over the actual basal in caloric intake is required to maintain nitrogen equilibrium. An important factor appears to be the clinical evidence of toxicity. In my opinion every effort should be made to give sufficient food to produce a gain in weight. A little special attention to the diet can usually bring this about. We are all familiar with the surgical disasters in the emaciated patient who is operated on when losing weight. In cases treated by X-ray or rest alone an adequate diet is of equal importance.

Associated with the disturbed nitrogen metabolism is the altered creatin-creatinin mechanism. In normal individuals on a creatin free diet no

creatin appears in the urine. The majority of the thyrotixicoses excrete considerable amounts of creatin. In a study of our 60 cases we have observed the excretion of over one grm. of creatin in 24° in several instances. Associated with the appearance of creatin is a lowered creatinin excretion. Usually the daily excretion of creatinin nitrogen is 7-11 mgms. per kilo; in the cases of exophthalmic goiter it is only 3-6 mgms. Prolonged feeding with a high caloric low protein diet will cause creatin to disappear from the urine. We have observed that from three to five days after the administration of iodine there is a spectacular decrease in the amount of creatin excreted, to either insignificant amounts or none at all.[2] No commensurate increase in the creatinin occurs. This effect of iodine on the creatin output does not seem to be necessarily dependent on the drop in the basal rate, for in some of our cases we have seen striking drops in the creatin with no change in the basal rate. In view of the suspected importance in normal metabolic function of the muscles in relation to creatin and creatinin the possible significance of this fact in the improvement can not be overlooked. After making these observations the discovery by Fishe and Subbarrow[3] and almost simultaneously by the two Egglestons[4] in Hill's laboratory, London, of the labile phosphorus-creatin compound increased our interest in the behavior of creatin in toxic goiters. The implication is that the phosphorus-creatin compound plays an important part in the normal function of muscle particularly in its tone and contractibility. One of the outstanding symptoms of hyperthyroidism is muscular weakness. It is impossible therefore to prevent the imagination from leaping ahead of our facts and wonder if in the thyrotoxicoses there may not be interference with the normal function of this newly discovered phosphorus compound.

Possibly linked with the abnormal creatin behavior is the low creatinin excretion. As you know, creatinin appears in the urine of normal individuals in constant amounts and is believed to be present in proportion to the active protoplasmic mass. So constant is the daily excretion of creatinin that it may serve as a check on the complete collection of 24 hour specimens for it is possible to detect the absence of a single voiding.

The above facts concerning the creatin and creatinin strengthen my belief that attention to the general nutrition is of great importance not only in preparation for operation but for care in general.

Now that the indiscriminate use of iodine in the treatment of thyroid disease of all sorts and descriptions is so prevalent it is rare for a case of Graves' disease to come to the clinic without the story of having taken iodine. Many times this is unfortunate since the strikingly good effect of iodine operatively is lost. In cases such as these the effect of iodine on the creatin excretion may be useful in the pre-operative stage. A case will illustrate the point. A Jewish school girl, 16, ill with Graves' disease for six months. For five months she had been taking iodine daily. At first she improved but for the past

four months no improvement, in fact her nervousness and palpitation have increased, and she has lost weight steadily. On admission there was marked restlessness, a high grade of exophthalmos, a large hard thyroid gland, pulse 140-150, a marked tremor and basal +61%. The iodine was stopped, she was given a creatin free diet of caloric value amounting to 100% in excess of her actual basal. The only drug employed was luminal /03 t i d. Within two weeks the situation was much improved. The gland was smaller and much less hard, the restlessness and tremor less marked and the pulse rate 110-120. She was gaining weight but the basal remained high +67%. She was excreting large amounts of creatin. As it was deemed advisable to remove part of the gland, iodine in the form of Lugol's solution was given in daily doses of 1 c.c. for 15 days and 3 c.c. for five days. After eight days the creatin disappeared but at the end of 19 days the basal metabolism was still high +54%. The improvement while taking iodine was definite but not marked. Partial thyroidectomy was done without incident. Similar cases have been observed and the question arises if the disappearance of creatin from the urine may not, in these cases that have received iodine before, serve as an indication of the optimum effect, of subsequent iodine administration.

The deviations from normal in the fat and carbohydrate metabolism are undoubtedly important but our knowledge does not at present permit of any significant practical use of the facts at hand.

Although the utilization of phosphorus and calcium is far from normal as shown by the increased excretion of these elements in thyrotoxic conditions and thyroid extract administration, and reflected in the diminished density of the bones, the clinical significance of these facts is not clear. We have had under observation in our wards for over a year a case of mild hyperthyroidism a s s o c i a t e d with marked disturbance in bone metabolism. In this particular case, which will be reported in detail by Dr. Turner or Miss Benedict later, the laboratory study of the calcium and phosphorus metabolism seems to have been of distinct service clinically. The patient is an unmarried girl of 19 who entered the Presbyterian Hospital in August, 1927, complaining of weakness in the legs and difficulty in walking. Her family history is good. During childhood she had measles and whooping cough. Influenza in 1918 and again in 1921. Possibly malaria in 1922. Septic sore throat, 1920. Tonsillitis, 1923, although the tonsils had been removed in 1915. She associated the onset of her present illness with the severe sore throat contracted in March, 1923. About a month after the sore throat her knees became stiff and she lost strength. For a few years she wandered from clinic to clinic, physician to physician, consulted osteopaths and chiropractors without relief. The stiffness of the knees and ankles increased, the wrists, elbows, and shoulders became involved. During this period she was treated for arthritis; received thyroid extract, pituitary extract, calcium, phosphorus; at one clinic a high basal (+25%)

was discovered and Lugol's solution was administered; various forms of light therapy, galvanic and faradic currents were employed.

On admission she was a poorly developed but fairly well nourished, good natured girl with difficulty of motion in her ankles, knees, wrists and elbows. The flexibility of spine was greatly decreased. She was unable to turn herself in bed. Eyes prominent but not true exophthalmus; thyroid gland not enlarged. No thrill or bruit. All ribs moderately tender on pressure. Heart negative except for over activity and rate varying between 100 and 130. Neither spleen or liver palpable. Marked tremor of the fingers and hyperactive reflexes. Blood and urine normal. Basal metabolic rate varied between +6 and +25%. Wassermann: Alcoholic antigen negative, Cholesterin +. X-ray of the bones revealed marked decalcification of all the bones. The epiphyses of both radii and ulnae ununited with disturbance at the epiphyseal margin. While the changes were suggestive of those seen in osteomalacia Dr. Golden felt they were not entirely characteristic. Furthermore, he noted in the right humerus evidence of periostitis and discovered a few areas suggestive of bone destruction, indicating possibly a luetic process. Further Wassermanns were taken with varying results—negative at times, + or + + at others. In view of the apparent derangement of the calcium and phosphorus metabolism she was transferred to the research ward and her Ca—P balances have been followed for over a year. Without subjecting you to the many details of the year's tedious work, the chief results demonstrate, I think, the importance of the studies in directing treatment. Her blood calcium was a low normal, her blood phosphorus distinctly low, 1 mgm. per 100 c.c. It was found that on a regular adequate diet she was constantly in negative phosphorus and calcium balance nor was this influenced by either sunlight or cod liver oil singly or combined, but when cod liver oil and 5 grms of calcium lactate were combined, she immediately established a distinct positive calcium and phosphorus balance. The blood calcium and phosphorus showed no change. There was also slight clinical improvement. Although there was no clinical evidence favoring syphilis the X-ray finding and the equivocal behavior of the Wasserman seem to justify a course of antileutic treatment. The calcium and cod liver oil were stopped and she received several doses of neoarsphenamine and mercury. The Ca—P balance immediately became negative and clinical improvement ceased with no change to be observed in the bones as shown by X-ray. On resuming cod liver oil and calcium by mouth the positive balance was re-established and she seemed to improve clinically, joints were less stiff, she could turn over in bed but there was little change to be noted in the X-rays. For six months she was kept on cod liver oil and calcium lactate with slow but steady improvement clinically and always in positive calcium and phosphorus balance. It was then determined to substitute ergosterol for cod liver oil. For two months this was combined with calcium lactate and two months without calcium. While combined with cal-

cium the effect seemed to be equivalent to the cod liver oil Ca combination, but when the Ca was omitted there was a gradual reduction in the amounts of Ca and P retained. Briefly, the result of her year's stay in the hospital has demonstrated the type of treatment which seems most effective. She is now able to walk with some difficulty about the ward, knitting, making baskets and in good nutrition. X-ray of her bones reveals a marked increase in the deposition of calcium as compared with those taken a year ago and there is an increase in the calcium deposits in the epiphyseal lines in several places.

The best clinical estimate we can make in this case is one in which there is mild hyperactivity of the thyroid gland combined with disturbed function of the parathyroids. The report I believe, serves to illustrate how the laboratory may aid the clinician in some of the difficult problems. Of course, cases such as this are rare but the importance of help to the individual is great.

I have made the attempt in the foregoing remarks to present my ideas concerning the relative values of certain laboratory aids, in the domain of metabolism, in the study and management of the thyrotixicoses. The impression I wish to leave with you is that while basal metabolism estimation, nitrogen studies and mineral balances may be of the greatest service, these aids are only safe if correlated with the general situation and their significance interpreted in the light of sound clinical judgment.

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The Delayed Type of Allergic Reaction*

Dr. Robert A. Cooke, *New York*

I THOUGHT it might be interesting to present, together with some illustrative cases, a type of hypersensitive reaction in man that has been little appreciated and is not well understood. The usual clinical conditions of asthma and hay fever are, generally speaking, immediate reactions; that is, the attack is precipitated very quickly within from one to thirty minutes after contact with the substance to which sensitiveness exists. In these cases the diagnostic skin test with this substance is also immediately positive, giving the typical urticarial wheal. It is in this group with the immediate clinical + test reactions that the sensitizing bodies are demonstrable by transfer of sensitiveness to normal human skin by means of the serum of a sensitive case. In this group also there is a great tendency to multiple reactions, that is, many clinical types of reaction, as well as reaction to many different substances. Here also we see a large group with positive antecedent family histories.

In contrast to this group, I want to call your attention to one that, for some reasons to be given later, seems properly to be classed as an allergic reaction. It, on the contrary, is characterized by the delay in the onset of the clinical reaction and by the absence of any cutaneous test. It appears chiefly in cases in which histories of antecedent allergy are not obtained and the reactions are usually single. At the present time the diagnosis is entirely a clinical one. I have selected four typical cases to illustrate the type of reaction to which reference is being made.

The first case was one of a woman, age 31, whose family history was entirely negative for all forms of allergy, and whose past history was negative for any other type of allergic reaction. This woman comes from North Carolina. In the fall, at the time when it is the custom to indulge rather largely in pork, she had for a period of several months eaten rather excessively of pork. At the end of two months she begin to have a generalized edema. This stopped within a few weeks after the ingestion of pork was stopped. At the end of several more weeks, not being thoroughly satisfied, she began again to use pork in smaller amounts, and the same reaction occurred, this time much more severe, so that there was a tremendous edema of the entire face, the eyes were tightly closed, and there was some edema of the larynx which obstructed breathing.

Two weeks later she had a similar attack after eating a small portion of

*Presented at the Boston Meeting of the American College of Physicians, April 10, 1929.

ham. In this case, following continued use, there was a definite increase in the sensitiveness of the individual to pork. In addition to the superficial angioneurotic edema, she had attacks of severe headache and abdominal pain that were probably of the same nature. There was, however, no manifestation of any asthmatic attack. Although in these cases treatment is not advisable, it was decided at least to determine by means of the intradermal test whether there was a sensitization or not, so that the test was made with the preparation of pork protein. The actual amount given is very, very small. There was no reaction at the site of the injection. Six hours later, however, there suddenly developed nausea, backache, abdominal pain, general prostration, a generalized pruritus, and urticaria with angioneurotic edema which passed off entirely in twelve hours.

A repetition of this test was done at the urgent request of the patient with identical results.

Another case was that of a school teacher, age 32, who had no previous sensitizations. When first seen she had a generalized urticaria which had been going on for a period of six months. A careful history of her habits and diet developed the fact that nearly at the time of the onset of this trouble chocolate had begun to be used in rather unusual amounts, at least unusual for her. The cutaneous reaction to a preparation of chocolate was done and it was entirely negative. It was two weeks after she stopped eating chocolate that the urticarial eruption entirely disappeared. Then following certain clinical observations, it was always possible after an incubation period of twenty-four or twenty-six hours to have a recurrence of urticarial lesions following the ingestion of the usual amount of chocolate. However, she could always take a reasonable amount, a quarter of an eighth of this, for an indefinite number of days without developing any reaction whatsoever. In other words, there is in this case, not only one of the typical delayed clinical reactions with absence of cutaneous reaction but a limit of toleration, a threshold beyond which she could not go without inducing symptoms.

A third case is that of a woman about 35 years of age. There was no antecedent history in her case and there was no personal history of allergy save for this particular thing. One night after she had eaten some soft clams and in two or three hours suddenly became nauseated and faint. Within a few hours there was a general urticaria and marked angioneurotic edema with headache and abdominal pain, but no vomiting and no diarrhea. Other individuals who had had the same meal and who had eaten the same thing had no symptoms whatsoever. In other words, it was not a type of ptomaine poisoning.

Two weeks before the patient was seen she had again eaten some soft clams for the first time in four years. In three hours there was a general urticaria, and this time no fainting occurred, but headache and abdominal pain were present as at first. The intradermal tests were done, with an extract of the soft clam. There was no immediate reaction to the test, but in the course of the six-hour period

there was considerable edema of the arm with itching and the development of a mild, general urticaria which passed off in fifteen hours.

A repetition of this test gave the same period of incubation, that is a delay in the reaction of at least six hours and a mild general reaction following, which lasted for a period at this time of six to eight hours.

The last case which I want to cite to illustrate this type of delayed allergy is that of a woman 31 years of age, who all her life had had a distinct sensitiveness for milk and eggs. They always produced a sense of nausea. They were taken, however, in small amount in cooked foods and in disguised form. Following the birth of her first child she was induced to take milk in amounts. Shortly after this began urticarial attacks which lasted until the diet was altered. On account, then, of the difficulty that she had in maintaining the proper nutrition, having become so extremely sensitive to milk, it was attempted to try to modify this by means of ingestion injection. Her sensitiveness, had developed to such a point that the equivalent of .0001 of a cubic centimeter of uncooked milk by subcutaneous injection would be followed by symptoms of urticaria and angioneurotic edema, and before the attack passed off, a short attack of asthma. This happened not on one occasion but on a number of occasions. In this case, the cutaneous tests with the milk were themselves absolutely negative, and the reaction time from the injection to the development of urticaria was from five to six hours.

In all of these four cases the sensitization has occurred—mind you, these are purely the striking cases that have been selected—to ordinary articles of diet, and reactions have followed the ingestion of quantities which, of course, would not produce any reaction at all in normal persons. It seems, then, perfectly justifiable to include these cases as a type of allergic reaction. The reactions also occur not only to foods but to drugs.

In these four cases there are several interesting features. In two of them the reactions have followed the use of these certain articles of foods over long periods of time, but in the other two cases, there has been no excessive use and the frequency of their administration has been minimal.

The other interesting point is the increase in the sensitiveness that has occurred, and in spite of this increase of sensitiveness there has been no appreciable shortening of the period of incubation, that is the period between the contact and the resulting symptoms. It seems proper to classify these cases as allergic on account of the typical clinical evidences of allergy reaction to common foodstuffs when taken in reasonable amounts. It may well be that a number of the cases that belong or are supposed to belong in the general group of allergic conditions are examples of the delayed reaction. Although there has been no proof as yet of the fact, it is the clinical experience of pediatricians that in certain cases of periodic vomiting definite improvement has been shown following the exclusion or the decrease in certain types of food in the diet.

As to the nature of the mechanism of this particular reaction, it is not known. One might be led to believe

that there was some analogy between it and serum disease. However, this analogy is not complete for the reason that although there is a delayed incubation period in serum disease at first, after serum disease, cutaneous reactions are possible and skin transfer of sensitiveness is also possible. So that we cannot at the present time assume that it is a form of induced sensitiveness analogous to serum disease.

As to the method that has to be pursued in the diagnosis of any case of this kind, of course it is obvious that in certain cases, as those cited, the reactions were either so intense or followed such an unusual type of food that the patient himself had made the diagnosis. But it is by no means necessary to stretch the imagination to suppose that many of our undiagnosed cases of allergic conditions belong in this same class and are not to be diagnosed by means of the immediate cutaneous reaction. The only resort that we can have at the present time is rather laborious and uncertain, one of variations in diet, the clinical method of trial and error.

My reason for presenting this paper is not only to bring forward an idea with regard to an unusual type of hypersensitiveness but to try to emphasize the difficulties that are inherent in this work. There are all sorts of combinations that may occur between the clinical reactions and the cutaneous tests. In those cases of immediate clinical reactions, we usually get an immediate positive cutaneous reaction, but there are immediate clinical reactions like asthma and hay fever in which the cutaneous tests may be entirely negative. Here, however, we can assume, and very properly, a localization of the hypersensitive area. In the cases where there is a delay in the clinical reaction, immediate cutaneous tests could not be expected to occur. There are also instances in which, without any clinical manifestations at all, positive cutaneous reactions occur.

It seemed to me that this was perhaps an excellent opportunity to emphasize not only the use but the difficulties with, and the abuse of the skin test in diagnosis of allergic conditions. I want particularly to call attention to the fact that skin testing is only one procedure in the diagnosis of hypersensitive conditions. It is by no means a hundred per cent fool-proof. The importance of a clinical study in allergy is just as great as are the tests themselves which must be used only as an aid, and a good deal of common sense must always be employed in their interpretation. They cannot be accepted on their face value. It is always wise to make a careful clinical study and use tests merely as a guide.

Serum Inorganic Sulphates In Addison's Disease

E. G. WAKEFIELD, M.D., *Fellow in Medicine, The Mayo Foundation, Rochester, Minnesota*

IT HAS been shown[2,3,5,6,7] that during the critical periods and terminal stages of Addison's disease renal insufficiency may be manifested and is evidenced by the retention of urea and by inability of the kidney to excrete water and phenolsulphonephthalein. The amount of total solids in the urine also may be lessened.

The object of my study was to determine if the concentration of serum inorganic sulphates is increased in Addison's disease. Also, if serum inorganic sulphates were found to be increased I hoped to establish whether the increase is a constant feature of the disease or whether it occurs only during the critical periods and in the terminal stages, or, if retention of serum inorganic sulphates occurs only during the critical periods and terminal stages of the disease, then I hoped to establish the relationship of retention of sulphates to renal insufficiency.

Patients who came to The Mayo Clinic and who were hospitalized for treatment of Addison's disease were studied. During their stay in the hospital, determinations of serum inorganic sulphates were made in duplicate on two days in all but two cases. The results are given in table 1. The sulphates were determined colorimetrically. As nearly as was possible, the conditions were kept constant. The diets were as constant as is possible in Addison's disease, for the diet is necessarily controlled by the capricious appetite of the patient.

In cases 4, 8, 11, 14, and 15 (table 1) there was an increase in serum inorganic sulphates. In case 8, blood for determination of sulphates was obtained on the day of death. In cases 3 and 5, the values (0.5 to 1.5 mg. in each 100 c.c.) are higher than normal values for serum sulphate but are no higher than those frequently seen in patients in hospitals (from 2 to 3.5 mg. in each 100 c.c.). In case 13 the value for urea was 49 mg. in each 100 c.c. and the value for creatinine 3.5 mg. in each 100 c.c. By more detailed analysis of cases 11 and 12, certain conditions will be identified which result in definite increases in serum inorganic sulphates.

In case 11, serum sulphates were definitely increased on the first determination. The patient manifested evidence of renal insufficiency. The concentration of urea in each 100 c.c. of whole blood was 106 mg. and of creatinine, 2.4 mg. Excretion of phenolsulphonephthalein was estimated as 35 per cent in two hours. After the

*Work done in the Division of Medicine under the direction of Dr. L. G. Rowntree. Submitted for publication July 31, 1929.

TABLE I
SERUM INORGANIC SULPHATES IN FOURTEEN CASES OF ADDISON'S DISEASE

Cases	First determination	Second determination
1	0.9	1.3
2	2.0	2.1
3	2.8	3.4
4	3.5	4.6
5	2.6	3.0
6	1.5	1.9
7	0.7	
8	4.1	
9	3.1	3.6
10	3.0	3.0
11	7.2	4.2
12*		
13	7.8	6.0
14	3.0	2.8
15	3.5	3.6

*Results are charted in figure 1.

patient had been in the hospital for about one week and had received fluids intravenously, as well as all that he could take comfortably by mouth, the concentration of urea in the whole blood dropped to 42 mg. and of the sulphates in the serum to 4.2 mg. in each 100 c.c.

The patient represented in case 12 remained under observation for thirty-two days. He was very ill and had frequent gastro-intestinal upsets, with periods during which there was a decrease in the urinary output. The relation of serum sulphates to the urinary output is shown in figure 1. In this case the concentration of blood urea was normal (20 mg. in each 100 c.c.). Excretion of phenolsulphonephthalein was 40 per cent in two hours. In figure 1 it is seen that the first determination of serum sulphate was made at the end of a period of four days during which less than 1 liter of urine was excreted daily. During this period the patient was very ill; he was nauseated and frequently vomited; that is, he had just gone through one of the gastro-intestinal upsets which are common in the course of Addison's disease. Synchronously with the cessation of vomiting, the output of urine rose rapidly, and there was general improvement in his condition. The volume of the urine perhaps was increased by the 2 liters of solution of glucose given on the two preceding days. In the next interval of five days, the daily output of urine remained well within normal limits. The concentration of serum sulphates gradually returned to normal. Then there was a relapse, the nausea and vomiting returned, the output of urine decreased and the concentration of serum sulphates rose. In the first part of this relapse, the patient had a reaction following the intravenous administration of solutions of glucose, so that for a few days thereafter none was given. On the twentieth day after admission, the administration of so-

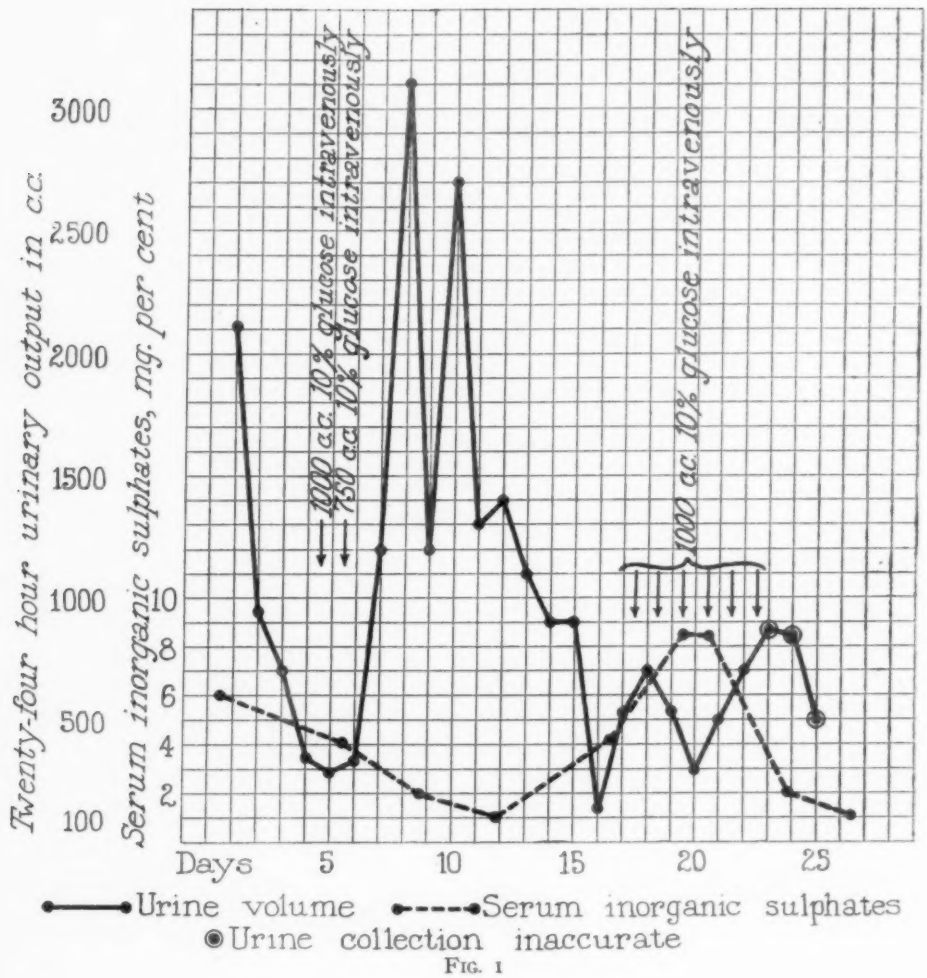

FIG. 1

lution of glucose again was started and 1 liter of a 10 per cent solution was given daily for about six days. The concentration of serum sulphates fell rather rapidly to normal. The patient was very ill, he became psychotic and it was difficult to get him to take fluids by mouth, although he was not nauseated and did not vomit. Likewise, it was impossible accurately to collect the urine.

COMMENT

Previously, in a study of the effect of diuresis on the concentration of serum inorganic sulphates, it was found that the diuresis from the administration of salyrgan caused a slight but definite decrease in levels of serum sulphate. Patients with edema of renal origin were studied. A further observation made at that time was that during the water and concentra-

tion tests of Volhard and Fahr, the only significant changes in the concentrations of serum sulphates were observed in cases in which there was definite gross renal insufficiency. Increases in the serum sulphates were found during the concentration test and decreases after the water diuresis. That is, fluctuations in concentrations of serum sulphates can be made to occur by controlling the urinary output, especially if there is impaired renal function. The rise in the concentration of serum sulphates in case 12, in this study, is comparable to that in a prolonged concentration test; the patient was unable to take the fluid instead of it being withheld.

The renal insufficiency in Addison's disease is not manifested except during the critical periods and the terminal stages of the disease. This fact probably is significant, for it is at these times that the asthenia is the most marked. Definitely to correlate the renal insufficiency with the vascular asthenia would be difficult, if not impossible, and was not attempted in this study. The difficulty of making such a correlation is appreciated when one recalls that the blood pressure already is so low in the typical case of Addison's disease that the margin left for it to fall and still be compatible with life is very small.

The critical periods of Addison's disease are accompanied usually by nausea and vomiting. Often the vomiting is severe enough to cause not only lowered daily urinary excretion but mild dehydration. The question then arises as to whether the increased concentration of sulphates and urea is not a condition comparable to that often seen in high intestinal obstruction. These two conditions are not the same, for the blood chlorides and the carbon dioxide combining power remain practically unchanged during the periods of vomiting in Addison's disease; whereas, in upper intestinal obstruction, altered values for the carbon dioxide combining power and chlorides may take place before any definite changes take place in the concentrations of the blood urea. From this evidence, it seems that renal insufficiency, probably from circulatory asthenia, is the important factor in the production of increased values for serum sulphates, and that if it were not for this renal insufficiency the amount of dehydration could hardly cause the increase in sulphates and urea so often seen.

Some experimental work on animals is cited which will help to establish the fact that impaired or suspended suprarenal function, with the subsequent circulatory asthenia, produces lowered renal function. In 1916, Marshall and Davis showed that when suprarenalectomized cats die, the urea content of the blood and tissues is much higher than that of normal animals. These experimenters made further studies, and found that after complete removal of the suprarenal glands, renal function was decreased in the interval before exhaustion and low blood pressure set in. Marshall and Davis did not determine the concentrations of the blood sulphates. In 1928, Swingle and Werner studied the chemistry of the blood after extirpation of the suprarenal glands in dogs and found that the inorganic sul-

phates may be greatly increased after such a procedure.

SUMMARY

Concentrations of serum inorganic sulphates are normal in cases of Addison's disease except during the critical periods and the terminal stages of the disease. The increase in the concentration of serum sulphates during these periods is an expression of renal insufficiency.

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Phosphorus In The Blood And Urine: A Study Of The Excretion And Retention Of Phosphorus In A Normal Subject And In Patients With Renal Disease*

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THE rôle of inorganic chemical compounds in the physiologic processes of man remains elusive. This paper is the report of studies on the significance of inorganic compounds of phosphorus as related, especially, to the urinary excretion in the normal person and in patients with renal injury. The effect of oral and intravenous administration of phosphatic compounds on the level of phosphorus in the blood and on the amount of urinary phosphorus excreted is studied in normal subjects and in patients with nephritis. An understanding of how frequently phosphorus is involved in almost all physiologic processes can be gathered from the very complete review by Forbes and Keith of all literature dealing with phosphorus as related to animal life. Bergmann showed that sodium phosphate injected subcutaneously into dogs appeared entirely in the urine and that the path of excretion was not altered even though the intestine was laden with calcium. He found, though, that in sheep the injected phosphorus appeared almost entirely in the feces.

Elias and Weiss injected solutions of phosphate intravenously in patients with diabetes and in normal control subjects in an investigation on the effect of phosphates on blood sugar. As far as I know, these are the only investigators who, up to the time of my work, have introduced solutions of phosphate directly into the blood stream of man. The effect of intravenous injection of solutions of phosphate has been studied mainly in animals, chiefly in dogs and rabbits. Binger, Salvesen, Hastings and McIntosh, and Tisdall were able to obtain a decrease in the level of calcium and an increase in the level of phosphorus on injection of solutions of sodium phosphate. They obtained tetany when using alkaline or neutral solutions. Lehman injected into rabbits for each kilogram of body weight from 50 to 75 mg. of phosphorus in the form of acid sodium phosphate. An immediate rise of the inorganic phosphorus in

*Abstract of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Medicine, March, 1928. This work was done in 1927 and 1928. Since then, similar work, but with organic phosphates, has been done by R. T. Bain and H. D. Kay, working in Arthur Ellis' Clinic at the London Hospital. Submitted for publication July 3, 1929.

the blood occurred and this was followed by a return to normal within four hours. He obtained tetany in some cases in spite of the fact that he used the acid salt. Addis, Meyers, and Bayer noted an immediate rise of the amount of phosphorus in the plasma and urine, with a gradual fall to normal or below. They used a solution of the acid and alkaline salts adjusted to a hydrogen-ion concentration of 7.4 and injected into rabbits an amount equivalent to 25 to 50 mg. of phosphorus for each kilogram of body weight. In 1872 Falck injected into dogs from 0.6 to 1.3 gm. of sodium phosphate for each kilogram of body weight. He obtained a peak in urinary phosphorus in between one and two hours after injection, and this was followed by a gradual fall, which reached normal in from six to nine hours after injection. Frey's experiments showed a continuing rise in the output of urinary phosphorus at three hours after injection, although the level of phosphorus in the serum had fallen remarkably by that time. Underhill injected neutral sodium phosphate into cats and found the greatest change in the plasma. He also noted that the rate of disappearance from the plasma is much slower for phosphorus than for either urea or creatinine. Iversen showed an immediate rise and a rapid fall of the level in the plasma after injection of phosphorus, but in the cells the level rose slowly and continued to rise when the level in the plasma was falling.

The significance of phosphorus in nephritis can well be measured by the large number of articles on this subject. Fleischer noted diminished excretion of phosphorus in nephritis with a change in the content of phosphorus of the feces. Kovesi and Roth-Schultz, as recorded by von Noorden, found almost constant retention of phosphorus in cases of nephritis; this was especially marked in cases in which edema was developing. The relation levels in the blood of inorganic phosphorus and of nonprotein nitrogen in nephritis were studied by Greenwald. He found that they usually ran parallel, but in isolated cases he obtained a high value for serum phosphorus with a low value for nonprotein nitrogen, or just the reverse. Denis and Minot noted a striking premortal rise in plasma phosphorus in all fatal cases of nephritis. In two nonfatal cases there was not a rise to alarming heights. They found no constant relation between retention of phosphorus and the amount of nonprotein nitrogen. In fact, in several of the fatal cases there was normal nonprotein nitrogen, whereas in cases in which the patients recovered the nonprotein nitrogen was high and the blood phosphorus and phenolsulphonephthalein return were n o r m a l. Twenty-two cases of nephritis and cardiorenal disease were reported by Denis and Hobson. Of these, there was increase of inorganic phosphorus in the blood in 45 per cent. Salvesen and Linder studied fifteen cases of Bright's disease. Uremia occurred in two of these and was associated with severe retention of phosphorus.

The significance of retention of phosphorus as a prognostic sign was noted by Schmitz, Rohdenburg and Myers. However, they found that the amount of creatinine ran parallel to

the retention of phosphorus and that the latter was as reliable a sign, if not more reliable, than the former. Their results disclosed a rather constant low level of calcium in the blood in patients with retention of phosphorus. DeWesselow reported eight cases in which the patients died with symptoms of uremia. In all of these there was severe retention of phosphorus, although the blood urea was not markedly elevated in all cases. On the strength of this observation, DeWesselow also considered that severe retention of phosphorus offered a grave prognosis. He noted that the levels of calcium were below normal in a high percentage of cases and suggested that the administration of calcium salts might have some therapeutic value. Marriot and Howland believed phosphorus to be the cause of acidosis in nephritis. They also advised administration of calcium as a means of eliminating phosphorus. This suggestion was based on the rather great frequency with which a low amount of calcium was found with retention of phosphorus and also on the observation that the ingestion of large amounts of calcium caused increased excretion of phosphorus in the feces. However, Bergmann previously had shown that in carnivora all the phosphorus in the stool comes from the phosphorus ingested and that calcium does not draw any phosphorus from the blood into the intestine. In this connection it might be well to mention the work of Boyd. She administered calcium chloride and calcium lactate to children with nephritis and brought about an improvement of edema. However, the calcium did not affect the blood phosphorus or the acidosis as suggested by Marriott and Howland. Halverson, Mohler, and Bergeim could find no effect of the administration of calcium in cases of uremia and severe nephritis, even though there was an associated low blood calcium. Fetter noted great retention of inorganic phosphorus in nephritis with acidosis and suggested that the phosphorus is retained to maintain the physiologic reaction of the blood. He believed that the retained phosphorus causes phosphorus acidosis and, in contrast to Marriott and Howland, suggested that this can be relieved by the administration of more phosphorus. One case is reported and in this he obtained favorable results with the treatment. Boyd, Courtney, and MacLachlan reported the results of two years' study on thirty-three cases of nephritis. Increase of plasma phosphorus was found in 66 per cent of cases and decrease of calcium occurred in 71 per cent. The inverse ratio of phosphorus to calcium was present only in cases in which the levels were far from normal.

Method of Experiments With Tabular and Graphic Representation of Results

The work here recorded may be divided into four studies. In the first, the output of phosphorus* in the ur-

*It should be noted that the determinations for phosphorus in the blood and urine were for inorganic phosphorus, and those for phosphorus in the feces were for total phosphorus. To avoid monotony in the paper, the unmodified term "phosphorus" has been used in many instances in which the concern has been with total phosphorus or with inorganic phosphorus.

ine, as described by Haldane, Wigglesworth, and Woodrow, was studied in a normal subject and in two patients with renal injury (tables 1, 2 and 3). This curve was followed only during the morning hours. After the previous evening meal, the subjects were not allowed to have food. Water was given in moderate amounts. Breakfast was withheld and a known amount of water, usually 500 c.c., was given at 8:00 a. m. Urine was collected hourly after 7:00 a. m. and until 12:00 noon. All specimens were measured and preserved with chloroform, whether they were examined

TABLE 1.—NORMAL OUTPUT OF PHOSPHORUS IN A HEALTHY SUBJECT UNDER CONTROLLED CONDITIONS*

	Urine				Blood			Plasma
		Phosphorus, mg.			Inorganic phosphorus, mg. in each 100 c.c.			
Hour	Volume, c.c.	In each c.c.	Each hour	$_pH$	Whole blood	Plasma	Serum calcium, mg. in each 100 c.c.	Carbon dioxide, combining power, per cent by volume
11 p.m. to 7 a.m.	240	1.07	32.1	5.7				
8 a.m.	35	0.59	20.8	5.5	3.27	3.37	10.0	67
9 a.m.	65	0.17	11.2	5.4				
10 a.m.	310	0.03	10.1	5.8	3.15	3.02	9.6	59
11 a.m.	68	0.17	12.0	5.5				
12 noon					3.02	2.89	10.3	59
12:20 p.m.	50	0.33	12.6	5.5				

*The subject did not have breakfast but drank 500 c.c. of water at 8 a.m.

TABLE 2.—OUTPUT OF PHOSPHORUS UNDER CONTROLLED CONDITIONS,* IN A CASE (CASE 1) OF CHRONIC GLOMERULONEPHRITIS WITH UREMIA

	Urine				Blood		
		Phosphorus, mg.			Inorganic phosphorus, mg. in each 100 c.c.		
Hour, a.m.	Volume, c.c.	In each c.c.	Each hour	$_pH$	Whole blood	Plasma	Serum calcium, mg. in each 100 c.c.
5 to 7:30	290	0.17	19.7	4.8	7.73	7.88	6.7
9:00	210	0.17	24.9	5.8			
10:30	170	0.18	20.7	5.4			
12 noon	190	0.16	21.3	5.6			

*The patient did not have food for fourteen hours but drank 250 c.c. of water every hour.

TABLE 3.—OUTPUT OF PHOSPHORUS UNDER CONTROLLED CONDITIONS,* IN A CASE (CASE 2) OF MALIGNANT HYPERTENSION WITH UREMIA

	Urine				Blood	
		Inorganic phosphorus, mg.				
Hour	Volume, c.c.	In each c.c.	Each hour	$_{p}H$	Inorganic phosphorus in plasma, mg. in each 100 c.c.	Serum calcium, mg. in each 100 c.c.
4 to 7:30 a.m.	60	0.25	3.8	6.6	7.4	8.9
9:00 a.m.	60	0.26	10.5	7.2	7.8	
10:30 a.m.	60	0.26	9.1	6.0		
12 noon	75	0.27	13.1	5.6	7.6	
1:30 p.m.	80	0.27	14.5	5.4		
3:00 p.m.	60	0.29	11.7	6.6		
4:30 p.m.	80	0.28	15.3	5.6		

*The patient did not have breakfast or lunch but drank 250 c.c. of water every hour.

immediately or not. The inorganic phosphorus, and in some cases the hydrogen-ion concentration, of each specimen was determined. For the latter, Gillespie's method, as described by Clark, was used. The hydrogen-ion concentration was studied to see whether any variation of the curves of phosphorus and of alkali occurred in cases of renal injury. In several cases the levels of inorganic phosphorus in whole blood and plasma were obtained to determine whether or not these changed with the curve of output. The blood urea, creatinine, serum calcium, inorganic phosphorus, and return of phenolsulphonephthalein were determined in every case of injury. This curve of the output of phosphorus obtained under the same controls as described here, was determined later in all cases in which sodium phosphate was administered. Thus, the curve of the output of phosphorus was determined for each subject, whether healthy or diseased. The name "control day" will be applied to this day on which the curve that was "normal" for each person was determined.

In the second series of studies, the effect was noted of oral administration of acid and alkaline sodium phosphate on levels of inorganic phosphorus in blood and urine. Two persons were studied, one a healthy subject (table 4) and the other a patient with chronic glomerulonephritis and subsiding uremia (table 5). A control day, preceding the day of administration of sodium phosphate was obtained for each subject. The same conditions were maintained on the day of administration. To the normal subject, 7 gm. of acid sodium phosphate, and to the nephritic patient, 12 gm. of the alkaline salt were administered early in the morning. The serum calcium and the inorganic phosphorus of the whole blood and of the plasma were determined before ingestion of the salt and at intervals thereafter. The urine was collected at hourly intervals and analyzed for inorganic phosphorus. The results

TABLE 4.—VALUES FOR PHOSPHORUS UNDER CONTROLLED CONDITIONS* IN A HEALTHY SUBJECT; OUTPUT OF PHOSPHORUS AND LEVELS IN THE BLOOD

Date, December	Hour	Urine: Volume, c.c.	Urine: Phosphorus, mg. In each c.c.	Urine: Phosphorus, mg. Each hour	Blood: Inorganic phosphorus, mg. in each 100 c.c. Whole blood	Blood: Inorganic phosphorus, mg. in each 100 c.c. Plasma	Blood: Serum calcium, mg in each 100 c.c.	Comment
27	8:30 a.m.	33	0.95	31.4	3.32	3.33		Control day
	9:30 a.m.	240	0.07	18.6				
	10:30 a.m.	750	0.02	15.7				
	11:30 a.m.	600	0.02	15.1				
	12:30 p.m.	160	0.12	20.4				
28	8:30 a.m.	30	0.64	19.4	4.25	3.70	10.8	7 gm. of acid
	9:15 a.m.	37	0.51	25.0	4.90	5.00	10.8	sodium phosphate
	10:15 a.m.	190	0.35	66.2	4.65		9.6	administered orally
	11:15 a.m.	510	0.14	72.8				at 8:45 a.m.
	12:15 p.m.	510	0.13	66.6	4.54	4.30	10.0	

*The subject did not have food for the preceding fourteen hours but drank 250 c.c. of water every hour.

TABLE 5.—VALUES FOR PHOSPHORUS UNDER CONTROLLED CONDITIONS* IN A CASE (CASE 3) OF CHRONIC GLOMERULONEPHRITIS AND SUBSIDING UREMIA

Date, December	Hour, a.m.	Urine: Volume, c.c	Urine: Phosphorus, mg. In each c.c	Urine: Phosphorus, mg. Each hour	Urine: pH	Blood: Inorganic phosphorus, mg. in each 100 c.c. Whole blood	Blood: Inorganic phosphorus, mg. in each 100 c.c. Plasma	Blood: Serum calcium, mg in each 100 c.c.	Comment
15	7:30	200	0.27	10.8	5.6	4.4	4.4	8.6	Control day
	9:00	45	0.33	9.9	5.2				
	10:30	90	0.32	19.2	5.4				
	12 noon	90	0.36	21.6	5.4				
16	7:30	260	0.32	16.6	5.6	4.8	4.7	8.2	12 gm. of alkaline
	9:00	80	0.46	24.4	5.2				sodium phosphate
	10:00	80	0.48	40.4	5.0	5.1	5.5	9.2	administered orally
	11:00	70	0.47	32.9	5.0				at 8:00 a.m.
	12 noon	110	0.37	40.7	5.8	4.7	5.1	8.9	

*The patient did not have food for fourteen hours but drank 500 c.c. of water at 7 a.m.

were charted and compared with those obtained on the control day. Later, 14 gm. of the salt was administered to the healthy subject (table 6). Urine was not obtainable because of the laxative effect. However, the levels of phosphorus in the blood were determined and charted.

TABLE 6.—THE LEVELS IN THE BLOOD OF INORGANIC PHOSPHORUS AND OF CALCIUM IN A HEALTHY SUBJECT

Hour, a.m.	Phosphorus, mg. in each 100 c.c.		Serum calcium, mg. in each 100 c.c.	Plasma
	Whole blood	Plasma		Carbon dioxide capacity, per cent by volume
* 8:30	3.62	3.10	10.6	67
9:30	4.52	5.03		57
10:30	4.26	4.83	11.0	61
11:30	4.11	4.39	10.6	56

*Ingestion of 14 gm. acid sodium phosphate.

Up to this point, the amount of inorganic phosphorus of the blood and of the urine was determined by the Briggs modification of Bell-Doisy's method. This method was not the most satisfactory, for the colorimetric solution faded too rapidly and only a small number of determinations could be made with each standard. For later studies, the method of Fiske and Sudbarrow was used. This proved to be accurate and allowed for more determinations to be run simultaneously because of the stable color of the solutions. With both methods, determinations of blood were run through immediately for it has been found (Zucker and Gutman and others) that the inorganic phosphorus undergoes changes when allowed to stand in whole blood, producing a higher level of phosphorus for whole blood and a lower level for plasma than really is present in vivo. The blood was centrifugalized immediately, hematocrit readings were taken, and the plasma was drawn off. Throughout, only the inorganic phosphorous was determined, except in the feces, in which determinations of the total phosphorus were made. The method for the determination of serum calcium also was changed. Earlier, the Tisdall modification of the Kramer-Tisdall method was used. For later studies, the Clark-Collip modification was used. Blood urea was determined with the Marshall method as modified by Van Slyke and Cullen. The method of Folin and Wu was used for the determination of blood creatinine. The level of uric acid in the blood was determined only a few times; the method described by Benedict was used. The carbon dioxide combining power of the plasma was determined by the volumetric method of Van Slyke and Stadie.

In the oral administration of sodium phosphate many factors are involved which interfere with the obtaining of consistent results. Chief of these are the rate and amount of absorption from the intestine and the laxative effect of the salt. This method of approach was discarded and an attempt was made to find a solution containing phosphorus which could be given intravenously with safety. A solution of sodium phosphate, here described, finally was developed and proved very satisfactory. A solution of acid sodium phosphate (9 per cent)

was added to a solution of alkaline sodium phosphate (9.6 per cent) in a ratio of three parts of the former to seventeen parts of the latter. By calculation and analysis, this contained 17.2 mg. of phosphorus in each cubic centimeter. This solution gave a hydrogen-ion concentration of 7.1 to 7.2 after being autoclaved. It was prepared in amounts of 200 c.c. and was kept in stoppered flasks of pyrex glass. The solution never was kept more than four days. Massive doses were injected into a dog without any symptomatic effect. Seventy-three cubic centimeters (400 mg. of phosphorus) was injected intravenously into a dog which weighed 11 kg. (table 7). Catheterized specimens of urine were taken every fifteen minutes and samples of blood were taken before injection and at intervals after injection. Three hours after the first injection, 55 c.c. (950 mg. of phosphorus) was given, also without noticeable effect. The blood and urine were examined for their content of inorganic phosphorus. Intradermal wheals of the solution of phosphate were not painful, so it was considered safe to attempt intravenous injection into a human subject. Starting with 5 c.c. at the first injection, the dose was increased daily until the maximal dose of 61 c.c. (1050 mg. of phosphorus) was reached. In a man who weighed 70 kg. this dose equalled 15 mg. of phosphorus for each kilogram of body weight. Ten minutes were taken to complete the injection and subjective effects were not noticed at any time. This rather large dose was more than two times the size of any dose given after this time, and was used only to give assurance that smaller doses could be administered with safety. The effect of injection of the solution of phosphate on levels in the blood and urine was not determined until a dose of 11.8 mg. of phosphorus for each kilogram of body weight was reached. The total for a man weighing 72.2 kg. would be approximately 852 mg. This was done on a healthy adult male. The conditions on the day of injection were controlled in a manner similar to that in which they were controlled on a preceding control day. The solution was injected at 8:15 a. m. Urine was collected at hourly intervals and analyzed for inorganic phosphorus and to determine the hydrogen-ion concentration. Blood was drawn before injection and at intervals thereafter.

TABLE 7.—CONCENTRATION OF INORGANIC PHOSPHORUS UNDER CONTROLLED CONDITIONS *IN URINE AND BLOOD IN A DOG WEIGHING 11 KG.

Hour, a.m.	Urinary phosphorus, mg. in each c.c.	Blood Phosphorus mg. in each 100 c.c.		Serum calcium mg. in each 100 c.c.
		Whole blood	Plasma	
**9:30	0.44	6.26	7.34	10.8
9:45	2.47			
9:50	3.62			
9:55	3.49			
10:00	3.09	12.2	12.4	
10:15	2.11			
10:30	2.15	10.3	11.3	9.2
10:45	2.43			
11:30	2.17	8.41	8.34	8.3

*The dog did not have food for fifteen hours; urine was collected by catheterization.

**Injection of 23 c.c. (400 mg. phosphorus) of solution of phosphate.

Determinations were made for serum calcium, plasma carbon dioxide combining power, and inorganic phosphorus of the whole blood (fig. 1).

In the third series of studies, this same subject was given a controlled weighed diet which contained a minimal and known amount of salts and he was allowed a fixed daily intake of fluid (table 8). The activity and meals were routine from day to day. The diet consisted of 2,500 calories, with 60 gm. of protein, 126 gm. of fat, and 266 gm. of carbohydrate. The total fluid in the food was 930 c.c. each day. In addition to this, 1,400 c.c. of fluid was taken in beverages and as water. The inorganic constituents of the diet in grams each day were as follows: sodium 0.72, potassium 2.83, magnesium 0.19, sulphur 0.71, iron 0.014, chlorine (as chlorides) 0.84, calcium 0.92, and phosphorus 0.93.

This diet was carried through for nine days. All feces and urine were collected and measured. The urine was collected at regular hours during

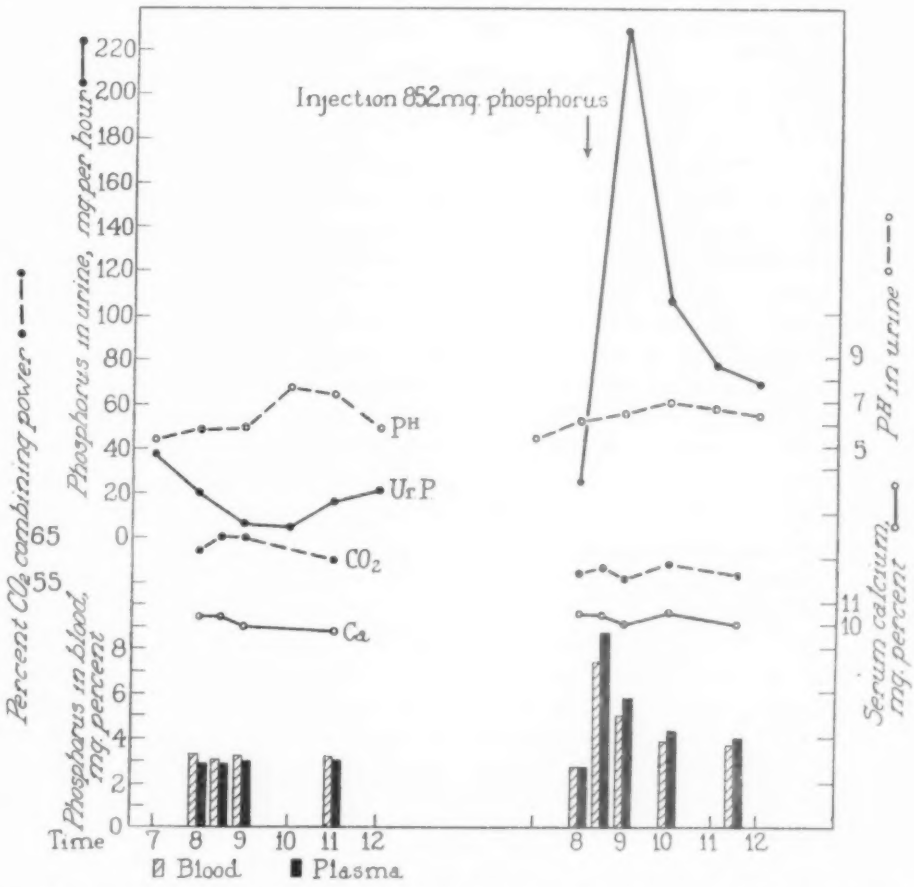

FIG. 1. The levels of constituents in urine and blood in a normal subject on a control day, and after injection of 852 mg. of phosphorus.

TABLE 8.—DAILY EXCRETION OF PHOSPHORUS AND CALCIUM IN THE URINE AND FECES OF A HEALTHY SUBJECT DURING A PERIOD OF CONTROLLED DIET

Date, December	Calcium, mg.			Phosphorus, mg.			Comment
	In urine	In feces	Total	In urine, inorganic	Feces, total	Ratio of phosphorus in feces to phosphorus in urine	
3 to 4	55	660	715	864	328	1:2.6	
4 to 5	60	836	896	1344	504	1:2.6	837 mg. phosphorus injected
5 to 6	56	566	622	795	307	1:2.5	
6 to 7	57	227	284	646	132		Small amount of stool passed
7 to 8	62	543	605	1468	495	1:2.9	875 mg. phosphorus injected

the day, and during the morning it was collected every hour. Each specimen was analyzed for hydrogen-ion concentration and for content of inorganic phosphorus, and the twenty-four hour total was analyzed for calcium. Every specimen of stool was examined for calcium and for the total amount of phosphorus. Injections of the solution of sodium phosphate were made on the fourth and seventh days. On these days, and on the third day, samples of blood were taken at intervals during the morning and determinations were made for serum calcium, carbon dioxide combining power, and phosphorus of the whole blood and of the plasma. On the eighth and ninth days, calcium lactate was given orally. On the ninth day this was followed by injection of solution of phosphorus. Several weeks later the same subject was placed again on the same diet for six days (table 9). During this period, 5 gm. of calcium chloride was given orally in solution on the second, third, and fifth days. On the fifth day, this was followed by intravenous injection of solution of phosphate. On the second, third and fifth days samples of blood were taken at intervals during the morning, after ingestion of calcium. The specimens of urine and stool were collected and treated as they were treated during the preceding period of diet.

The method of analyzing the feces should be described. The stools were passed into weighed porcelain dishes, were dried over a steam bath, and the weight of the dried material was noted. This was allowed to cool and then was pulverized. Of this powdered material, 0.25 gm. was accurately weighed out on a clean watch glass and washed into a hard glass nitrogen tube with from 3 to 4 c.c. of water. To this was added 2.5 c.c. of concentrated sulphuric acid. The tube, with its contents, was placed in a steam bath for from eight to twelve hours. This procedure breaks up the larger particles, and a thick black "so-

TABLE 9.—DAILY EXCRETION OF PHOSPHORUS AND CALCIUM IN URINE AND FECES OF A HEALTHY SUBJECT DURING SECOND PERIOD OF DIET

Date January	Calcium, mg.			Phosphorus, mg.			Comment
	In urine	In feces	Total	In urine, inorganic	Feces, total	Ratio of amount in feces to amount in urine	
5 to 6		1251					4.4 gm. calcium chloride orally
6 to 7	130	1002	1132	884	286	1:3	5.2 gm. calcium chloride orally
7 to 8	60	407	467	945	121		
8 to 9	120	1941	2061	1814	762	1:2.4	5.2 gm. calcium chloride orally, 1050 mg. phosphorus intravenously (unusually large amount of feces excreted)

lution" is formed. After several glass beads had been placed in the tube to inhibit "bumping" it was held over a micro-burner and was allowed to heat slowly to a point at which the solution bubbled gently. Care was taken that it did not boil vigorously. After about fifteen minutes of this heating, concentrated nitric acid was added drop by drop until the solution was clear. Heating and the addition of nitric acid were continued until the solution was colorless and clear. This was then washed into a volumetric flask with a capacity of 50 c.c. and water was added to the mark. From 2 to 5 c.c. of this solution was then analyzed for phosphorus according to the method of Fiske and Subbarrow. Molybdate solution II was used and was found to be more efficient than molybdate solution III. The amount of phosphorus found in 50 c.c. of solution equalled the amount in 0.25 gm. of dried feces. The total amount in the specimen could be calculated from this. The method of digestion here described was very satisfactory and proved to be accurate under several checks.

The fourth series of studies was performed on subjects suffering from renal disease. Figures 2, 3, and 4 are illustrative of these. This involved the injection of the phosphate solution intravenously. In view of the apparent nontoxicity, as found in the previous injections into a healthy subject, the solution was considered safe enough to administer to patients with renal injury and retention of phosphorus. The solution was administered to determine the rate and amount of phosphorus which could be excreted through the kidneys as compared with the output in a normal subject. Therefore, eleven subjects, ten patients with renal disease and one healthy subject were included in this series. An equivalent of 6.5 to 6.6

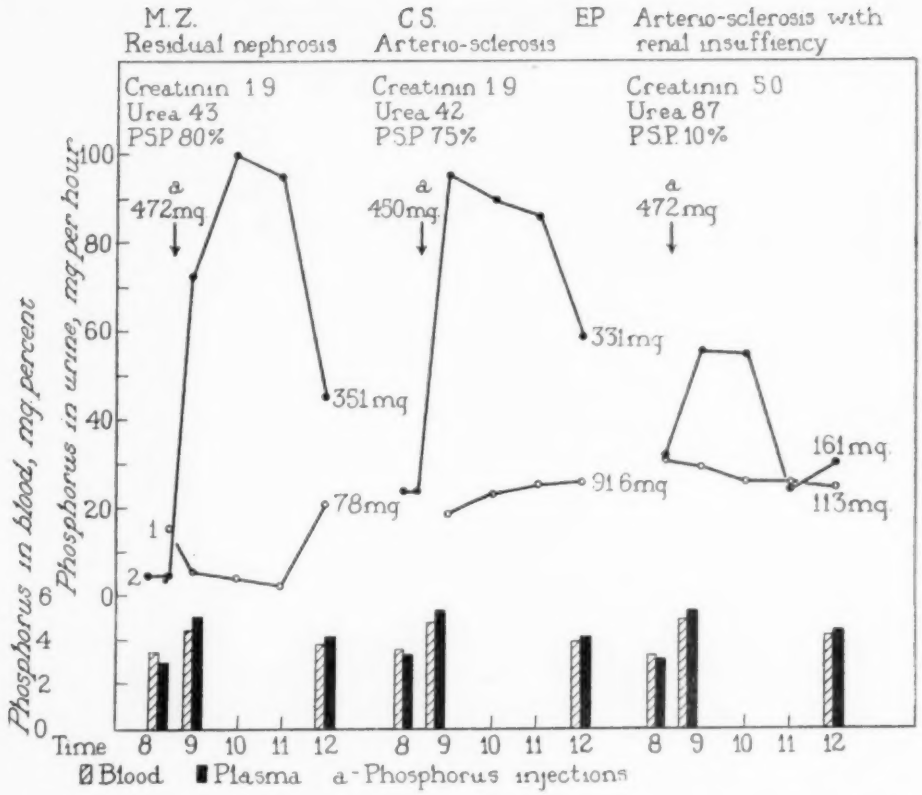

FIG. 2. Values for phosphorus and other constituents in three patients with renal disease (*M.Z.*, *C.S.*, and *E.P.*) in this figure and cases 4, 5 and 6 in table 10. (1) Output of phosphorus in urine on a control day. (2) Output of phosphorus in urine and levels of phosphorus in blood before and after injection of solution of phosphate.

mg. of phosphorus for each kilogram of body weight was injected into seven of the patients and the one healthy subject. In the remaining three patients, the dose was still further reduced to 5.1 and 5.5 mg. for each kilogram of body weight because of the rather marked retention of phosphorus that was present. Conditions were kept the same as those of the control days which preceded the day of injection in each subject. Food was not allowed after the evening meal. Five hundred cubic centimeters of water was taken at 7:30 a. m. and 250 c.c. more at 10:00 a. m. Urine was collected at 7:00 a. m. and at 8:00 a. m. The solution was injected at 8:10 a. m. Samples of blood were taken before injection and at intervals after injection. Urine was collected hourly until 12:00 noon, at which hour the last sample of blood was withdrawn. Complete chemical studies of the blood were performed on the first specimen of blood. Serum calcium, carbon dioxide combining power, and inorganic phosphorus of the whole blood and of the plasma, were determined on every sample.

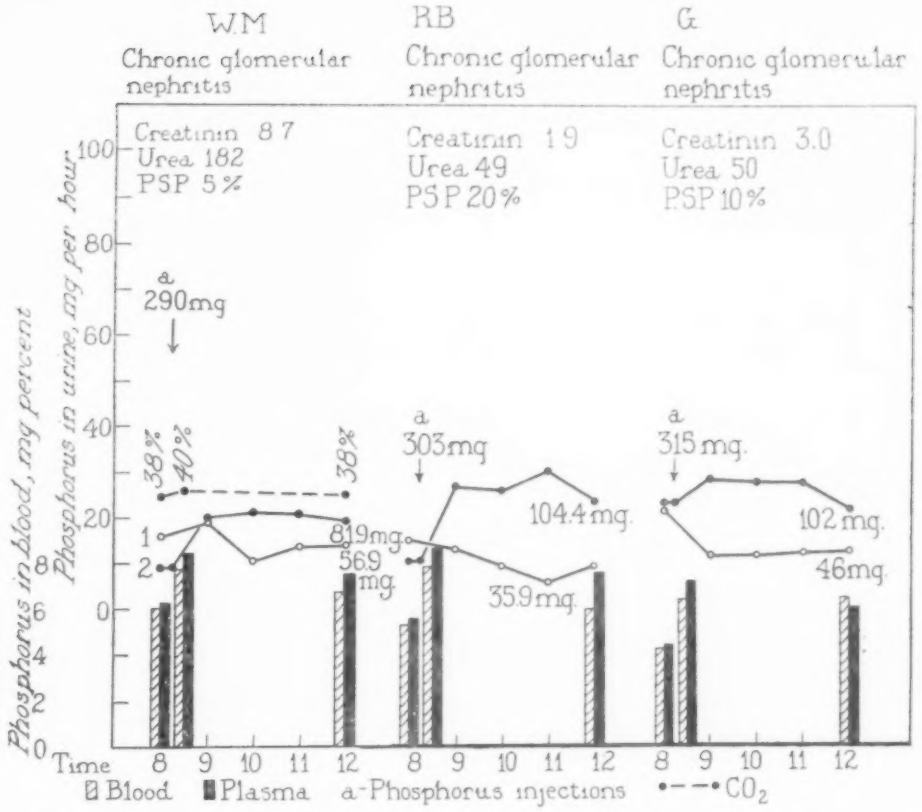

FIG. 3. Values for phosphorus and other constituents in three patients with chronic glomerulonephritis (*W.M.*, *R.B.*, and *G.*) in this figure and cases 8, 9 and 10 in table 10. (1) Output of phosphorus in urine on a control day. (2) Output of phosphorus in urine and levels of phosphorus in blood before and after injection of solution of phosphate.

The amount of inorganic phosphorus in each specimen of urine was determined. The total amount of inorganic phosphorus in all the urine passed after injection was ascertained and compared with the total obtained on the control day for the same hours. The difference between the two was taken as the amount recovered of the phosphorus which was injected. This offered some idea as to the percentage of excretion of phosphorus in various degrees of renal injury.

DISCUSSION

From the studies here presented and from those of investigators previously alluded to, it will be accepted that retention of phosphorus in the blood frequently occurs in nephritis. Many theories have been advanced as to the cause of retention of phosphorus, its significance from the standpoint of prognosis and treatment, and its relation to the symptoms and to the results of studies on the chemical constituents of the blood in ne-

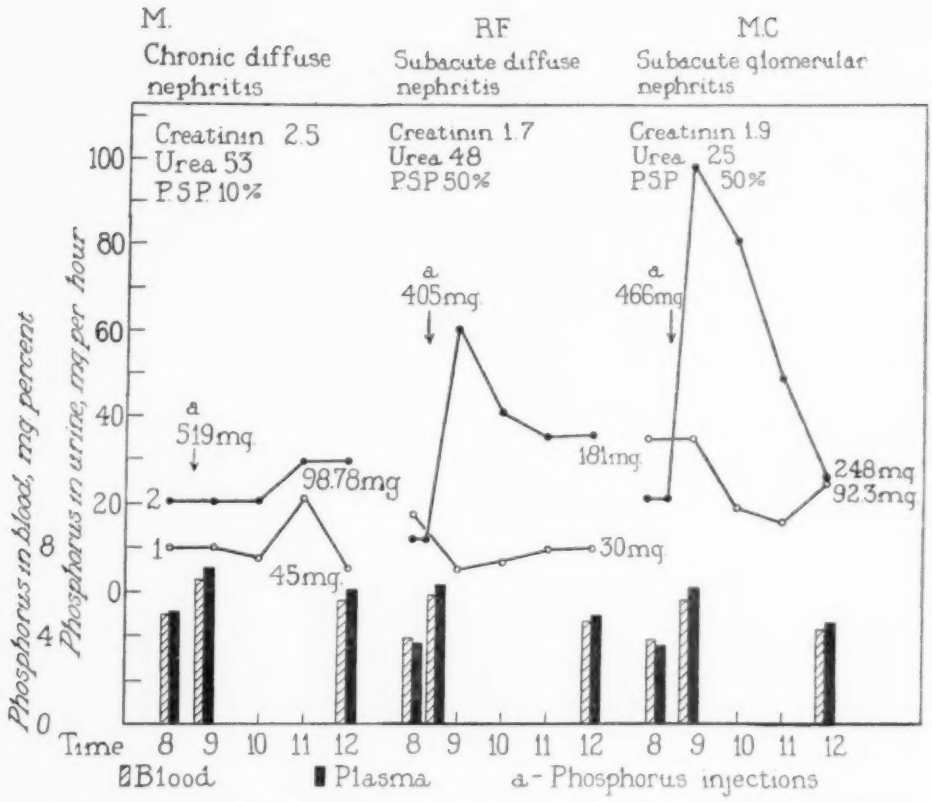

FIG. 4. Values for phosphorus and other constituents in three patients with subacute and chronic nephritis (*M.*, *R.F.*, and *M.C.*) in this figure and cases 11, 12 and 13 in table 10. (1) Output of phosphorus in urine on a control day. (2) Output of phosphorus in urine and levels of phosphorus in blood before and after injection of solution of phosphate.

phritis. Many experiments have been described, and observations reported, to throw light on this subject. The studies and results described in this paper are an attempt to add to the knowledge of metabolism of phosphorus in health and in renal disease.

The normal level of inorganic phosphorus in the blood is from 2.5 to 4.0 mg. in each 100 c.c. In a normal subject, the levels in the plasma and in the cells are probably the same. As a rule, it is found that the level in the plasma is lower than that in the whole blood. It is known that, if whole blood is allowed to stand, the inorganic phosphorus diffuses into the cells. Zucker and Gutman obtained a value for phosphorus in the cells two times that of the value for phosphorus in the plasma after they had allowed blood to stand five hours or more. By the time the blood has been centrifugalized and the plasma drawn off, some diffusion already has occurred; thus a higher value for inorganic phosphorus in the whole blood would be obtained. In my observation of the normal subject, the level of inorganic

phosphorus always was a trifle higher in the whole blood, even though determinations were made immediately.

In cases of nephritis with retention of phosphorus this is not found true. The value for phosphorus in the plasma is consistently higher in these patients. In table 10 are found seven cases in which retention of phosphorus in the plasma was more than 4.0 mg. in each 100 c.c. In case 2, determinations were not made on the whole blood. Only in case 3 was the level of phosphorus in the whole blood equal to that in the plasma. In cases 1, 8, 9, 10, and 11, the level of phos-

TABLE 10.—RÉSUMÉ OF RESULTS OF CHEMICAL EXAMINATION OF THE BLOOD IN THIRTEEN CASES OF RENAL INJURY. ALSO A COMPARISON OF THE RETURN OF INJECTED PHOSPHORUS WITH THE RETURN OF PHENOLSULPHONEPHTHALEIN

Case	Inorganic phosphorus mg. in each 100 c.c.		Plasma		Whole Blood			
	Whole blood	Plasma	Carbon dioxide capacity, per cent by volume	Serum calcium, mg. in each 100 c.c.	Creatinine, mg. in each 100 c.c.	Urea, mg. in each 100 c.c.	Return in urine of injected phosphorus, per cent	Return in urine of phenolsulphonephthalein, per cent
1	7.7	7.8	32	6.7	14.0	233		
2		7.7		8.9	9.8	238		10
3	4.4	4.4	34	8.6	3.8	85		30
4	3.4	3.1	50	10.2	1.9	43	59	80
5	3.5	3.4	54	10.8	1.9	42	55	75
6	3.2	3.2	53	11.2	5.0	87	10	10
7	3.9	3.8	57	10.4	3.7	62	25	25
8	6.0	6.3	38	9.7	8.7	182	9	5
9	5.3	5.5	47	7.6	1.9	49	22	20
10	4.2	4.3	47	9.3	3.0	50	17	10
11	5.0	5.09	51	8.7	2.5	53	10	10
12	3.9	3.8	46	9.3	1.7	48	37	50
13	3.7	3.5	63	10.6	1.9	25	33	50

phorus in the plasma during fasting was higher than that in the whole blood. The difference is more marked when the retention of phosphorus is greater. The same proportion was found in many other cases not recorded here. This would indicate that some abnormal mechanism, possibly the same as that which produces the retention, has a tendency to hold the phosphorus in the plasma.

The suggestion often has been made that the retention of phosphorus is closely related to acidosis. Some have maintained that the retention is the cause of the acidosis; others have felt that the retention is the result of the acidosis. My results are not conclusive evidence that the two are related. In cases 1, 3, and 8 (table 10) the carbon dioxide combining power was below 40 volumes per cent. There were severe phosphorus retention and high blood urea in cases 1 and 8. In the other case (case 3), there was only mild retention of both phosphorus and

urea. On the other hand, in cases 9, 10, and 11, in which also there was retention of phosphorus, there was no evidence of acidosis. These cases, also, exemplified only slight retention of urea.

The level of serum calcium seems to have a closer relationship to content of phosphorus than does the carbon dioxide combining power of the plasma. In seven cases of retention of phosphorus, five (cases 1, 2, 3, 9, and 11) were associated with a value for serum calcium below 9.0 mg. in each 100 c.c. In the one case (case 8) in which there was severe retention of phosphorus there was a calcium level of 9.7 mg. in each 100 c.c. A value for serum calcium of 9.3 mg. in each 100 c.c. was obtained in two cases, in one of which (case 12) the value for phosphorus in the serum was normal and in the other of which (case 10) there was retention of phosphorus. Five patients with renal disease in whom the value for phosphorus was normal also had a serum calcium above 10.0 mg. in each 100 c.c. Apparently Boyd was correct in her conclusion that the inverse proportion of calcium to phosphorus exists only when the levels are far from normal. There occurred but one exception to this (case 8) in my series.

Study of the levels of creatinine given in table 11 demonstrates that retention of phosphorus is frequently associated with a high concentration of creatinine in the blood. Among eight patients (cases 1, 2, 3, 6, 7, 8, 10, and 11) with an elevated value for creatinine, there was retention of phosphorus in six. These six died of nephritis within four months of the time of examination. One patient (case 6) who did not have the associated retention of phosphorus also died. One patient (case 9) with retention of phosphorus had a normal value for creatinine. This patient and the one (case 7) with a high value for creatinine, without retention of phosphorus, did not die. In chronic nephritis it will be admitted that retention of creatinine and of phosphorus usually offers a fatal prognosis. However, I agree with Schmitz that creatinine furnishes the more reliable sign.

It has been stated often that retention of phosphorus is always associated with retention of urea. Several investigators, however, have shown that patients may have severe uremic symptoms without real retention of urea. In these cases they have found marked retention of phosphorus, and have attributed the symptoms entirely to the retained phosphorus. Even though this is accepted as true, my results do not give evidence of such a conclusion. Retention of urea occurred in all patients with an elevated value for creatinine. Three cases with retention of urea, without an increase in inorganic phosphorus, are represented in table 11 (cases 6, 7, and 12). In two of these (cases 6 and 7) there was retention of creatinine. Only case 6 was fatal and in that the value for creatinine was 5.0 mg. in each 100 c.c. of blood.

The concentration of phosphorus varies considerably in the urine if the renal function is normal. In a normal subject, after injection of phosphorus, the concentration in each cubic centimeter of urine was 6.4 mg. In cases

4, 5, 12, and 13 (table 10), the concentration was above 1.0 mg. in each cubic centimeter. In nephritis of the glomerular type, with definite renal injury, there occurs a tendency to fixation of concentration of phosphorus, depending on the degree of injury. This is seen in tables 2, 3, and 4 where the concentrations are charted. In these and in cases 6, 7, 8, 10, and 11 in table 10 the urinary concentration of phosphorus never was higher than 0.5 mg. in each cubic centimeter. In case 9, in which renal disease was definite, the concentration was 0.76 mg. in each cubic centimeter. One would suspect that injury to the kidney, as in case 9, would alter the curve of the output of phosphorus as obtained in the normal subject by Hawk and Chamberlain and others. I obtained this curve in the normal subject, both when the subject was fasting and when he was receiving the diet low in salt, and also in patients with nephritis. The output of phosphorus in the normal person was independent of diuresis. A suggestion of the curve is seen in tables 2, 3, and 4, but the amount of phosphorus excreted each hour is wholly dependent on the amount of urine passed.

The cause of the type of curve of the output of phosphorus, as it occurs in the normal subject, has not been determined. The best explanation seems to be that based on the work of Marshall and Crane. They show that the variation in output of urinary constituents is dependent, to a greater or less degree, on the rate of flow of blood through the kidneys. This could account for the "alkaline tide"[27,29] and for the curve of the output of phosphorus. It is significant that the two occur at the same hours (table 1). It was suggested at one time that the change in the output of phosphorus was due to a change in reaction of the blood and urine. However, it has since been shown that the two are independent of each other. Ingestion of sodium bicarbonate increases the alkalinity of the blood and urine without perceptible change in the levels of phosphorus in either blood or urine. It is also found that intravenous administration of the solution of phosphate increases levels of phosphorus in urine and blood without change in the alkaline tide. The carbon dioxide capacity of the plasma also shows little change after the injection of phosphorus.

A picture of the path of excretion of phosphorus and calcium can be obtained by studying a subject on a controlled diet containing a known amount of the substances that are to be measured in the excreta. With the diet described, there occurs no alteration of the curve of the output of phosphorus or of the alkaline tide. In table 8 it can be noted that the excretion of calcium through the urine is fairly constant from day to day. The amount of calcium excreted in the feces depends on the amount of stool passed in one day. Calcium is one of the main constituents of feces and one of the factors controlling the contents and consistence of it. As a rule, the amount of the calcium in the feces is ten to twelve times that in the urine. The intravenous injection of the solution of phosphate does not affect the amount of calcium excreted in the stool. When additional calcium is

taken orally it is immediately reflected by a considerable rise in excretion of calcium, in both urine and feces (table 9). This added calcium apparently is excreted within twenty-four hours, as the excretion for the following day is not above the normal. The oral administration of calcium produces a mild increase in the level of serum calcium.

The daily output of inorganic phosphorus in urine, when the subject was on the diet, ranged from 646 to 864 mg. The total amount of phosphorus in the feces depends somewhat on the amount of stool passed but is always less than the amount of phosphorus taken orally and much less than the amount excreted in the urine. The ratio of the total amount of phosphorus in the feces to the urinary inorganic phosphorus is found to be from 1:2.5 to 1:2.9. This is not affected either by the injection of phosphorus or by the administration of additional calcium by mouth. The intravenous injection of the solution of sodium phosphate produces an increase of phosphorus both in the urine and in the feces. There is an immediate increase in the output of the phosphorus in the urine. The injected phosphorus is excreted within twenty-four hours or less, for on the following day the output is normal. However, part of the injected phosphorus apparently is lost. This probably occurs through absorption into the tissues and does not amount to more than from 6 to 12 per cent of the amount injected.

The total amount of phosphorus in the feces is increased after injection but is less than that which is taken orally in the food. One cannot say whether the increased amount of phosphorus is due to excretion from the blood, or whether the absorption from the intestine is inhibited because the level of phosphorus in the blood is so high. The feces were passed from four to five hours after injection of the phosphorus and must have been fairly low in the intestinal tract at the time of injection. Thus it would appear that the increased amount of phosphorus in the feces was due to excretion from the overladen blood. When the work of Bergmann is considered it must be admitted that some excretion probably does occur. He found, after subcutaneous injection of solution of sodium phosphate, that in carnivora all the injected phosphorus appears in the urine even though the intestine is laden with calcium; in herbivora, on the other hand, the injected phosphorus is excreted almost entirely through the feces. Man, an omnivorous animal, should show some of the characteristics of both and thus should be able to pour phosphorus from the blood into the intestine, especially when the blood is laden with phosphorus in a diffusible form.

It has been suggested in cases of retention of phosphorus that oral administration of calcium would cause excretion of additional amounts of phosphorus through the stool and thus the phosphorus which the diseased kidneys could not excrete would be eliminated. Boyd has shown since that treatment with calcium in cases of nephritis in no way affects the elimination of phosphorus. The ingestion of calcium chloride does not

affect the levels of phosphorus in either urine or blood. The curve of urinary output of inorganic phosphorus retains the same shape it had when the subject was receiving the diet only. The ingestion of calcium chloride for two successive days does not produce a perceptible change in the excretion of phosphorus in either the urine or the feces over a period of twenty-four hours (table 9). The total amount of excreted phosphorus is the same as that when neither calcium nor phosphorus was administered. The ratio of the total amount of phosphorus in the feces to the total amount of inorganic phosphorus in the urine (1:3) is not materially altered from the normal. The intravenous injection of phosphorus following ingestion of calcium chloride produced a mild laxative action. In this instance the intestine was loaded with calcium at a time when the level of inorganic phosphorus in the blood reached the extremely high point of 9.09 mg. in each 100 c.c. It would be expected that this phosphorus could be removed easily for it is in a very diffusible form. This state, it would seem, would make it adaptable to the influence of the calcium in the bowel, the effect of which would be to draw the phosphorus to the intestine. The results one would think, should be reflected in a very marked increase in the excretion of phosphorus in the feces, with the increase of the amount in the urine not as great as that which occurred when only phosphorus was given. These phenomena did not appear. In table 9, it is shown that the largest amount of the injected phosphorus appears in the urine. The amount of inorganic phosphorus that is excreted, above the normal amount, is almost as much as the amount injected. There does occur a decided increase in the total amount of phosphorus in the feces but no more than would occur if only phosphorus were given. The ratio of the total amount of phosphorus in the feces to the amount of urinary inorganic phosphorus, which on one day was 1:2.4, is not remarkably lower than that which was obtained on days when only the phosphorus was administered. There is no suggestion in these results that the calcium in the intestine draws any more phosphorus to it even when the blood is laden with phosphorus above a normal level. Therefore, if these results are true, one can say that the ingestion of calcium does not alter the path of excretion of phosphorus in cases of retention of phosphorus, and the calcium does not have therapeutic value in cases of nephritis from that standpoint.

It has been previously stated that in the normal person the level of inorganic phosphorus in the plasma is the same as that or lower than that in the cells. Also, in cases of retention of phosphorus due to nephritis the level in the plasma is higher than that in the cells. It has been shown that the injection of a solution of phosphate intravenously into a normal subject produces a marked rise in the levels of inorganic phosphorus in the blood. The greatest increase occurs in the level in the plasma, which becomes higher than the level in the cells and retains this position until the levels approach normal. The injection of phosphorus seems to have

no effect on the level of calcium in the serum. The carbon dioxide combining power of the plasma does not diminish after the injection of phosphorus. In fact, there is a tendency toward an increase. This was found to be true, also, in cases of nephritis, whether or not it is associated with retention of phosphorus and acidosis. The significant fact is that reduction of the alkali reserve does not occur.

Studies on the normal subject have shown that the increase in the level of phosphorus in the blood is reflected in an immediate and very prominent increase in urinary excretion of inorganic phosphorus. The peak of excretion occurs within the first hour. This is followed by a gradual fall in output, which approaches normal after four hours. The amount of phosphorus excreted in a fasting subject between the hours of eight and twelve in the morning would be fairly constant from day to day. The figure thus obtained could be subtracted from the amount of phosphorus excreted after injection of solution of phosphate under the same circumstances. The difference, in milligrams, would give an indication of the amount of injected phosphorus that was recovered. The amount recovered would depend on the renal function and would offer some idea of the amount of injury to the kidney, if the return were less than that obtained in the normal subject. About 59 per cent of the phosphorus injected is recovered within four hours, in a normal subject. Excretion of phosphorus is diminished in renal disease. A résumé of the amounts recovered in all the cases is given in table 10. A striking feature is the parallelism which occurs in cases of severe nephritis between the return of phenolsulphonephthalein and of phosphorus. As the phenolsulphonephthalein approaches normal, the return of phosphorus remains a little lower. The results would indicate that a return of from 40 to 50 per cent of phosphorus is to be expected from a normally functioning kidney. A return of less than that is indicative of renal injury; the less the return, the greater the injury. The patients (cases 6, 8, 10, and 11) in whom the return of phosphorus was less than 20 per cent died within four months. It is also to be noted in figures 3 and 4 that in cases of severe nephritis the peak of urinary excretion of phosphorus after injection does not occur during the first hour as in the normal subject but is delayed for from one to three hours. It can be concluded from these results that in cases of nephritis the recovery of injected phosphorus depends on the extent of renal injury, and that the urinary response to injection of phosphorus is much delayed when renal function is very low.

Summary

Studies were made of the levels in the blood and of the urinary excretion of inorganic phosphorus in the normal person and in subjects with nephritis. A solution was made of the acid and alkaline sodium phosphates and this was balanced to a hydrogen-ion concentration close to that of the blood. This solution was very satisfactory for intravenous injection into dog and man; subjective effects were not noted. The path of

excretion of phosphorus was studied by administering to a normal subject a controlled diet which contained a minimal and known amount of mineral. The daily total amount of phosphorus in the feces and the amount of inorganic phosphorus of the urine were determined. The effect of intravenous injection of the solution of phosphate on the levels of phosphorus in the blood or the amount excreted in feces and urine was studied. In addition, the effect was noted on the levels of calcium in the blood, on the amount of calcium excreted, and on the acidity of blood and urine. Calcium chloride was given orally in doses of from 4.5 to 5.0 gm. to determine if calcium altered the path of excretion of phosphorus in any way. It was concluded that calcium does not draw any phosphorus from the blood into the intestine, even when the blood is laden with phosphorus. A standardized dose (6.6 mg. for each kilogram of body weight) of phosphorus was injected into a healthy subject and into patients with nephritis to determine how much of the injected phosphorus would be recovered in the urine within four hours after the injection. It was discovered that in subjects with normal renal function, the return was 50 per cent or more. In the presence of renal injury, the return was lessened depending on the amount of injury to the kidney.

Conclusions

1. In a normal, fasting individual the level of inorganic phosphorus in the plasma is equal to or less than the level in the whole blood. In patients with nephritis in whom there is retention of phosphorus the level of inorganic phosphorus in the plasma is greater than that in the whole blood.

2. Retention of phosphorus associated with retention of creatinine in patients with chronic nephritis offers a fatal prognosis.

3. A mixture of solution of acid sodium phosphate, 9 per cent, and of solution of alkaline sodium phosphate, 9.6 per cent, in a ratio of three parts of the former to seventeen parts of the latter is suitable for intravenous injection into man. It is nontoxic. The intravenous injection of this solution produces an immediate rise followed by a gradual fall in the inorganic phosphorus of the blood; the level of phosphorus in the plasma is greater than the level in the cells; it causes an increase in the amount of inorganic phosphorus excreted in the urine and in the amount of phosphorus excreted in the feces; the amount in the urine is much greater than that in the feces. The carbon dioxide combining power of the plasma, the level of serum calcium, and the amount of calcium excreted in the feces are not appreciably affected by injection of the solution of phosphate.

4. In the normal, fasting subject 50 per cent of the injected phosphorus is recovered in the urine within four hours. In cases of nephritis, the urinary response is delayed and the amount of phosphorus recovered is decreased as the amount of renal injury is increased. Also, the return of the level of inorganic phosphorus in the blood to that preceding injection

is slower in patients with nephritis than in the normal subject.

5. In a normal person more phosphorus is excreted in the urine than in the feces. The ratio of the total amount of phosphorus in the feces to the amount of inorganic phosphorus in the urine is between 1 :2.5 and 1 :2.9 inclusive. The path of excretion of phosphorus is not altered by the ingestion of calcium chloride even though the level of inorganic phosphorus in the blood is raised through intravenous injection of solution of phosphate.

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The Long Interval Versus The Short Interval Treatment Of Hay Fever

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A REVIEW of the great volume of work that has been done since Wolf Eisner suggested that the symptoms of Hay Fever resembled the phenomena of experimental anaphylaxis, discloses the fact that we today are confronted with some of the same problems that baffled the pioneers in this study, to-wit:

1. Is Hay Fever a manifestation of anaphylaxis?

A number of workers including Dunbar,[1] Koessler,[2] Hall,[3] Alexander,[4] Parker[5] and Huber[6] support this view; while in direct opposition are listed the findings of Coca,[7] Cooke,[8] Grove and Coca,[9] Black[10] and Black and Moore.[11]

2. In group reactions of pollens does desensitization with the predominant member of the biologic group causative of the seasonal attack, protect against all members of that group?

Cooke and Van der Veer,[12] Scheppegrell[13] and Goodale[14] affirm this statement. Their contention is that the chief proteins of the pollens of one group are identical and that the symptoms are produced by contact with that protein. To further support this view Wells and Osborne[15] proved that when tested anaphylactically the chemical relationship of similar tissues of a group parallel the biologic relationship. Brown, [16] Watson and Kibler[17] and Bernton[18] take exception to this view. They agree that a certain amount of specificity exists; but contend that this conception does not explain satisfactorily many observed irregularities.

3. What is the best extraction medium in the preparation of pollen antigen?

The variance of opinions is best demonstrated by a review of the different methods. Noon and Freeman[19], credited as the first to devise a method of desensitization against Hay Fever, prepared their solution by alternately freezing and thawing the pollen in distilled water. After filtration the extract was boiled in sealed tubes. Clowes[20] precipitated pollen with acetone. Lowdermilk[21] substituted physiologic sodium chlorid solution for the distilled water. Clock[22] used a fluid consisting of 33 1/3 per cent saturated sodium chlorid and 66 2/3 per cent glycerole. Koessler[2] used an 8.5 per cent solution of sodium chlorid and he sometimes precipitated with 95 per cent alcohol, 10 times the volume of the pollen. Goodale[14] soaked grains in water for a few hours and added alcohol sufficient to make the dilution

from 13 to 15 per cent by volume. Walker[23] used 12 per cent alcoholic solution. Rackermann[24] added to physiologic sodium chlorid a slight amount of alkali in the form of 1 per cent normal sodium hydroxid. Coca[25] also utilized an alkali medium, consisting of sodium chlorid and sodium bicarbonate in such concentration that 10 c.c. of the final fluid equaled about 3 c.c. of a N/10 alkali. Duke[26] modified Clock's method by substituting Cocoa's solution for the saturated sodium chlorid solution. All extracts were sterilized by passage through Berkefeld filters. Phenol, trikresol and glycerol were employed to preserve the potency and maintain the sterility of these extracts.

4. What is the method of choice in the preseasonal desensitization against Hay Fever?

Walker's schedule of treatment has been followed with slight modification by most workers. This method consists of determining the threshold of reactivity by testing cutaneously with various dilutions of the causative pollen, viz., 1:10,000; 1:5000; 1:1000 and 1:500. In the average case the patient would react with a 1:5000 or a 1:1000 solution. Treatments would begin with the dilution next to that which gave the last reaction, giving 2, 4 and then 6 minims of each dilution at 5 or 7 day intervals until the maximum dose of 6 minims of the 1:500 solution were given. Duke[26] further modified this method by administering pollen extracts once or twice a day for the lesser concentrations and continuing at 24 to 48 hour intervals, governed solely by the degree of local reaction following the preceding dose. This method has aroused considerable interest.

The presented study was undertaken for the purpose of determining the relative value between what shall hereinafter be referred to as the long interval treatment advocated by Walker; and the short interval treatment reported by Duke. In addition some of the findings in this series may add weight to the evidence for or against some of the uncertainties heretofore enumerated.

With this purpose in mind patients presenting themselves for treatment of the Fall type of Hay Fever in May or June were started on the long interval treatment; while those who reported on June 20th or thereafter received the short interval type of treatment. Members of both groups were tested with two commercial diagnostic pollen preparations. Positive reactions to various members of the compositae family were obtained in all cases of clinical Hay Fever. These reactions occurred with about equal intensity with both of the preparations. For the long interval treatment an aqueous solution was used in dilutions of 1:10,000; 1:5000; 1:1000; 1:500 and 1:100. After determining the threshold of sensitivity by the dilution tests; 2, 4 and 6 minims of each dilution were administered, terminating the treatment with 6 minims of the 1:100 solution. Glycerolated pollen antigen was administered in the group receiving the short interval treatment. This is a 66 2/3 per cent glycerol and 33 1/3 per cent saturated sodium chlorid preparation consisting of 15 individual doses, with 2½ units in the

first dose and ending with 3000 units in the 15th dose.*

The comparative results given by the two types of antigen are shown in Charts A and B.

A comparison of Charts A and B shows that although the short interval treatment was begun from one to four weeks later, an average of 17 doses was administered against an average of 13 plus doses. Using a glycerolated pollen antigen preparation, the initial dose was 2½ units. A maximum of 3000 units was reached by rapid increases. This dose may be repeated, if indicated, at 4 day intervals as is shown in cases 3 and 11. Very little difference in the degree of local reactions and no constitutional symptoms resulted in those receiving the short interval treatment; while within 5 minutes following the prescribed injection of pollen, two patients in the long interval group developed angioneurotic edema with shortness of breath, wheezing, etc.—true bronchial asthmatic attacks requiring the administration of epinephrin to overcome the reaction. The results in spite of the short series are very encouraging. Excluding all patients that had more than an occasional sneeze, 5 (41+ per cent) were practically free from symptoms. Omitting all patients except those having an occasional paroxysm of sneezing and occasional itching of the eyes, etc., 4 (33+ per cent) were markedly improved. Three patients (25+ per cent) who still had symptoms of Hay Fever, were at least 50 per cent relieved as compared with previous seasonal attacks. In the long interval group 4 (18+ per cent) were practically relieved of symptoms; 9 (40+ per cent) were markedly improved; 7 (31+ per cent) were improved and 2 (9+ per cent) were failures.

Ephedrin, not used in any cases of this series, has been disappointing in the treatment of Hay Fever. Some relief is obtained before the onset of severe symptoms, but when fully established ephedrin is practically useless. Two factors seem important enough to report:

1. Ephedrin, even in small doses, may have a hypnotic effect in some cases. A child of 5 years of age was given 1/32 of a grain every 3 hours. After 3 doses the child slept an unusual number of hours. This effect may be due to impurities in the preparation of the drug.

2. There is a rapid development of tolerance to the drug. The same child, using the same tablets, could in one month take ½ grain of ephedrin without relief or untoward symptoms.

Recapitulating: Excellent results were obtained in 74 plus per cent of cases in series A with no absolute failures; while in Series B satisfactory results were obtained in 59 plus per cent cent with two failures. Koessler[2] in 1914 reported 36 cases of hay fever treated, of which 11 plus per cent were entirely relieved and 22 plus per cent were failures. Walker[25] in 1921 reported 22 per cent of a series of 202 cases entirely relieved of symptoms and 6 plus per cent failures. Cooke and Van der Veer[28] reported

*Better results are obtained when Hay Fever sufferers who have a bronchitis or who give a history of previous attacks of bronchial asthma, receive an autogenous vaccine from the nose or sputum, in conjunction with the pollen extracts throughout the period of treatment. This was not done in this series, thereby avoiding conflict in the conclusions to be drawn from the results obtained as to what the beneficial factors were.

CHART "A" (Therapeutic)
Short Interval Treatment.

Patient	Sex	Treatments Began	Treatments Ended	Number of Treatments	Interval	Z Reactions Local	Z Reactions General	95-100	80-95	50-80	50% & less
1. J.F	M	July 1	Aug. 16	30	Daily	1-2+	None	X			
2. B.Y.	F	Aug. 1	Aug. 16	15	Daily	1-2+	None	X			
3. W.F.	M	July 20	Aug. 16	18	1-4 days	1-2+	None			X	
4. A.F.	F	July 20	Aug. 16	18	1-4 days	1+	None	X			
5. M.K.	M	Aug. 1	Aug. 15	15	Daily	1-3+	None	X			
6. P.D.	M	Aug. 1	Aug. 15	15	Daily	2-3+	None		X		
7. G.D.	M	July 20	Aug. 14	15	1-2 days	2-3+	None		X		
8. J.G.	M	July 25	Aug. 14	15	1-2 days	2-3+	None		X		
9. A.N.	F	July 28	Aug. 14	15	Daily	3+	None		X		
10. C.M.	F	Aug. 1	Aug. 16	15	Daily	1-2+	None			X	
11. R.L.	F	July 24	Aug. 15	18	1-4 days	1-2+	None	X			
12. A.B.	F	Aug. 1	Aug. 15	15	Daily	1-2+	None			X	
								5 or 41+%	4 or 33+%	3 or 25+%	

Remarks: Case 1 had 15 daily doses ending July 16 and 15 additional doses ending August 16.
Case 3 had daily doses for 15 days followed by 3 maximum doses at 4 day intervals.
Case 7 omitted a day occasionally when local reactions had not subsided.
Case 11 had 15 daily doses then the maximum dose every 4 days for 3 doses.
Lederle's Glycerolated Pollen Antigen used in this group.

CHART "B" (Therapeutic)
Long Interval Treatment.

Patient	Sex	Treatments Began	Treatments Ended	Number of Treatments	Interval	Z Reactions Local	Z Reactions General	95-100	80-95	50-80	50% & less
1. F.O.	M	June 15	Aug. 16	13	5 days	1-2+	None			X	
2. E.D.	F	June 15	Aug. 16	13	5 days	1-2+	None	X			
3. F.K.	F	June 1	Aug. 14	16	5 days	1-3+	None	X			
4. L.O.	M	June 5	Aug. 15	15	5 days	1-2+	None		X		
5. M.O.	F	June 15	Aug. 18	13	5 days	1-3+	None		X		
6. C.H.	F	June 5	Aug. 16	15	5 days	1-3+	None			X	
7. B.U.	M	June 10	Aug. 18	14	5 days	1-3+	None	X			
8. S.S.	F	June 15	Aug. 15	13	5 days	1-2+	None		X		
9. M.F.	F	June 15	Aug. 15	13	5 days	1-2+	None				X
10. H.J.	F	June 10	Aug. 15	14	5 days	1-4+	Ang. Neu. Edema		X		
							Br. Asthma			X	
11. J.S.	M	June 12	Aug. 15	14	5 days	1-2+	None				
12. I.L.	M	June 15	Aug. 15	13	5 days	1-2+	None			X	
13. B.L.	F	June 12	Aug. 18	13	5 days	1-4+	Ang. Neu. Edema		X		
							Br. Asthma			X	
14. H.S.	M	June 15	Aug. 15	13	5 days	1-2+	None				
15. H.B.	M	June 14	Aug. 15	13	5 days	1-2+	None	X			
16. H.O.	F	June 15	Aug. 15	13	5 days	1-3+	None				X
17. A.M.	M	June 20	Aug. 17	12	5 days	1-3+	None		X		
18. R.R.	M	June 18	Aug. 15	12	5 days	1-2+	None		X		
19. A.D.	F	June 16	Aug. 15	12	5 days	1-2+	None		X		
20. C.C.	F	June 14	Aug. 15	12	5 days	1-2+	None		X		
21. C.A.	F	June 18	Aug. 14	13	5 days	1-3+	None			X	
22. P.O.	M	June 15	Aug. 16	13	5 days	1-2+	None			X	
								4-18+%	9-40+%	7-31+%	2-9+%

Arlington Chemical Company's aqueous solution used in this group.

Z

One plus—An erythema or wheal approximately ½ centimeter in diameter.

Two plus—Same as one plus except - centimeter in diameter.

Three plus—Same as one plus except 1½ centimeters in diameter.

Four plus—Same as one plus except 2 centimeters or more in diameter.

1,774 patients treated between 1916 and 1920—25 per cent were entirely relieved and 10 per cent were failures. The results obtained in series A with glycerolated pollen antigen compare favorably with the report of Clock[29] who obtained relief of symptoms in 84 per cent of 1,578 cases, using a similar preparation.

The foregoing indicates that a staple pollen antigen is requisite to the best results. The increased efficiency of our present day methods in preseasonal desensitization is due to two factors:

1. The marked increase in the concentration of a pollen content.

This can readily be seen by the fact that only 3 years ago, the maximum dose of commercial water soluble pollen protein was a 1:500 solution. These commercial houses as a routine now advise 1:100 solutions as a maximum dose. Those firms marketing a glycerolated pollen solution sell a preparation containing 3,000 to 4,000 pollen units as their maximum dose, as against 1,000 units of a few years ago.

2. The increased stability of glycerolated pollen antigen.

This was shown by Clock who found no loss of complement binding capacity in his preparation after 14 months. Bernton corroborated this finding and further proved that evidence of clinical potency is no indication of the original activity of the preparation. Using his own alcoholic saline pollen solution, comparing same with glycerolated pollen antigen pre-

Chart "C" (Etiologic)
Short Interval Treatment.

Patient	Age of Onset	Age First Seen	Heredity	Operations for Hay Fever*	Complications
1. J.F.	15	23	Asthma	2	Br. Asthma
2. B.Y.	40	50	Hay Fever	1	
3. W.F.	58	61			
4. A.F.	49	51	Asthma		
5. M.K.	19	23	Asthma		
6. P.D.	36	49			Br. Asthma
7. G.D.	31	51	Asthma		Br. Asthma
8. J.G.	24	31	Asthma	2	Br. Asthma
9. A.N.	43	51			
10. C.M.	28	36	Asthma	1	Br. Asthma
11. R.L.	20	24	Asthma	2	
12. A.B.	15	35	Asthma Eczema		Br. Asthma
Average	31+	40+	9 or 74+%	5 or 41+%	6 or 49+%

*No benefit derived from the operation.

Three plus—Same as one plus except 1½ centimeters in diameter.
Four plus—Same as one plus except 2 centimeters or more in diameter.

pared by the method of Clock, he found that his preparations showed a marked loss of antigenic properties, tested by the complementing fixation method as devised by Clock, after a period of 4 months while the glycerolated pollen antigen retained its original antigenic properties.

A composite form of the charts shows that 9 cases of series C and 7 cases of series D, a total of 16 cases (47+ per cent of the entire series), gave a history of some form of allergy, including Hay Fever, Asthma, Urticaria and Eczema in some direct antecedent. Six cases of series C and 9 of series D gave a history of attacks of Bronchial Asthma during previous seasonal attacks. These facts plus the occurrence of angio-neurotic edema

CHART "D" (Etiologic)
Long Interval Treatment.

Patient	Age of Onset	Age First Seen	Heredity	Operations for Hay Fever*	Complications
1. F.O.	30	61			
2. E.D.	34	46	Asthma	2	
3. F.K.	38	42	Hay Fever		Br. Asthma
4. L.O.	2	6		1	
5. M.O.	40	44			
6. C.H.	14	18			Spring and Fall Type
7. B.U.	28	34	Hay Fever	1	Br. Asthma
8. S.S.	27	28	Asthma		Br. Asthma
9. M.F.	15	36			
10. H.J.	24	27			Br. Asthma
11. J.S.	23	36	Hay Fever		Spring and Fall Type
12. L.L.	26	46		1	Br. Asthma for 40 years
13. B.L.	15	23	Asthma	2	
14. H.S.	30	41			
15. H.B.	18	33			Spring Type Urticaria
16. H.O.	19	23			Br. Asthma
17. A.M.	34	36			Br. Asthma
18. R.R.	12	22			
19. A.D.	35	48	Asthma	1	Br. Asthma
20. C.C.	39	44			Br. Asthma
21. C.A.	34	39			
22. P.O.	26	61		1	
Average	25+	36+	7 or 31+%	7 or 31+%	9 or 40+%

*No benefit derived from the operation.

CHART "E"
Composite of Charts "A, B, C and D"†

		Sex		Average Age						
		M	F	Onset	First Seen	Duration	Fam. Hist. of Allergy	History of Asthma Complicating Previous Seasonal Attacks	History of Nasal Operations For Relief*
Series A									
(12)	C	6	6	31+	40+	9+ years	9 or 74+%	6 or 49+%	5 or 41+%
Series B									
(22)	D	10	12	25+	36+	11+ years	7 or 31+%	9 or 40+%	7 or 31+%

*No benefit derived from the operations.

†All cases reacted to Ragweed, short and Ragweed, giant. In addition they reacted to one or more of the following pollens: goldenrod, sunflower, Russian thistle, cocklebur, yellow dock and corn.

and Bronchial Asthma in two cases following therapeutic injections of pollen, as noted on Chart B, make it difficult to separate Hay Fever from the category of anaphylactic conditions. It is noteworthy that, although all the cases reacted to many members of the compositae group productive of the fall type of Hay Fever and in spite of the fact that all the groups were treated with the combined Ragweed, short and giant Ragweed pollen, the results have been excellent. It therefore appears that treatment with the predominant member of the biologic group, especially if the predominant member gives the predominant reaction, will suffice for the treatment of seasonal Hay Fever. It will be observed that 12 cases (35+ per cent of the entire series) gave a history of one or more nasal operations that were performed to relieve their Hay Fever without a single instance of benefit resulting therefrom. It appears then that operative work without an absolute indication other than Hay Fever is a useless procedure.

Comment: The short interval treatment of Hay Fever has many advantages:

(a) Desensitization can be established within a relatively short period, two or three weeks. This statement must be modified, for the peak of pollenation is so great in some localities that weekly treatments throughout the season, with the maximum dose, seems advisable in order to obtain the best results. Dake and Durham[30] have shown a wide variability in pollen concentration in various cities, which justifies this procedure. They have shown that the count of pollens at the peak of the ragweed season in Chicago in 1925 was 500 pollens covering an area of 55/100 square inch, while in Kansas City it reached the tremendous number of 4,500, and in Oklahoma City, 7,200. These findings demonstrate the necessity of accurate knowledge of the pollenation curve for the

proper management of Hay Fever sufferers in any community. In New York City the maximum rarely reaches above 100 pollens per 55/100 square inch. Therefore, I deem it unnecessary to continue treatment after the onset of the season; except where the patient was not sufficiently desensitized prior to the season, or in the case of a highly sensitive patient, who in previous years had not received complete relief with the aforementioned procedure.

(b) Local reactions following treatments appear greater with the long interval treatment. Some of the wheals assume the proportion of a silver dollar and are accompanied by constitutional symptoms. The local reactions in those receiving the short interval treatment were less severe and in most instances had disappeared sufficiently so that subsequent doses could be given. In no instance in this series was it necessary to omit more than one day because of the local reactions caused by the preceding dose. The reaction usually reached the maximum within 15 minutes and had subsided sufficiently so that the patient was permitted to leave the office in 30 minutes.

(c) The pollen treatment sets used in the season of 1928 were of the same lot as those used in 1927, having been kept in the icebox for the entire year. The results in 1928 were no different from those in 1927, indicating that there was practically no loss in the potency of the extracts during that period of time.

Conclusions:

1. The intensive or short interval treatment seems the method of choice in the treatment of Hay Fever.

2. Hay Fever with the hereditary background and the frequent complications of Asthma, Urticaria and Angioneurotic Edema cannot be excluded from the category of Allergic Diseases.

3. Treatment with the predominant member of a biologic group of pollens causative of seasonal Hay Fever, is sufficient to care for the entire biologic group. Where more than one biologic group is present in sufficient concentration to cause symptoms, a combination of the predominant members of such groups is advisable for good results.

4. Best results are obtained with glycerol pollen antigen. This preparation retains complete potency for considerable periods of time.

5. Nasal operations with Hay Fever as a primary indication are worse than a useless procedure.

6. Ephedrin in the treatment of Hay Fever has proven disappointing.

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Brittle Bones And Blue Sclerae. Report Of A Case With Glycosuria

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THE recognition of the familial occurrence of brittle bones and blue sclerae is credited to Eddowes[1], although this association of abnormalities was reported by Spurway[2] four years earlier. Later, Bronson[3] and Van der Hoeve and de Kleijn[4] called attention to the hereditary association of otosclerosis and labyrinthine disease with deafness in the affected families. The syndrome is usually transmitted by the female, though it may be transmitted by the male. A number of affected families has been reported; the articles by Bronson[3] and Key[5] are accompanied by extensive bibliographies. Since the latter publication, additional families have been studied by Moller[6] and Paal[7].

Besides the hereditary occurrence of the syndrome of pathological fractures and blue sclerae, isolated cases have been reported in which no hereditary influence could be elicited from the family of the affected member. Bronson,[3] Herrman,[8] Ostheimer,[9] Gutzeit[10] and others, and recently, Hein [11] have reported instances of the sporadic appearance of this condition. Hein traced 23 members of a family in four generations without discovering another case. The authors' case seems to belong to this category. Hereditary and non-hereditary cases present the same clinical picture.

Report of Case

A girl, aged 4 years, 4 months, was seen April 1, 1929. The complaint was frequent fractures of the bones of the arms and legs.

The family history was essentially negative, except for the fact that a paternal uncle suffered from a neurological condition and had been unable to walk since he was a young man. A normal brother had died at 15 months of age of diphtheria. No other case of brittle bones or blue sclerae had been heard of in the families of the father or mother. Both parents were living and well.

Except for the presence of blue sclerae, the patient had seemed normal at birth, but at six weeks of age the right humerus was fractured. At one year there were multiple fractures of both femurs, and from this time, on an average of every six months, there was a fracture of an arm or leg. Abnormality in shape and development of the thorax was first noted at one year. Appetite had always been capricious and very poor, and there had been frequent attacks of nausea and vomiting from unknown cause. The first teeth had erupted at eight months. Mentality was normal.

Physical examination: Weight, 22½ pounds (10.2 kg). The patient was unable to walk, but got about upon a small contrivance with wheels, propelling herself with her feet. The musculature of the extremities was flabby and atrophic. The head was

quite large in proportion to the body, and seemed to rest directly on the thorax. The thorax showed a combination of pigeon-breast and barrel shape, its lower borders resting on the brim of the pelvis. The abdomen was protuberant. There was moderate flexion of the thighs and the legs could not be straightened. The sclerae were deep slate blue in color. The fundi were normal on ophthalmoscopic examination. The teeth were well formed and in good condition. There was moderate hypertrophy of the tonsils. The remainder of the examination revealed normal findings.

Laboratory examinations: Red blood cells, 4,020,000; hemoglobin, 70 per cent (Dare); white blood cells, 7,750. Differential white cell count: neutrophilic leukocytes, 60 per cent; lymphocytes, 28 per cent; monocytes, 12 per cent. The stained smear showed a normal picture. The blood Wassermann and Kahn reactions were negative. Serum calcium was determined on three occasions with readings of 13.0, 12.9 and 11.7 milligrams per cent (Clark and Collin's modification of the technic of Tisdall and Kramer); accompanying the last calcium determination the blood phosphorus was 4.4 milligrams per cent (technic of Fiske and Subbarow). The fasting blood sugar was 73 milligrams per cent (venous blood, technic of Folin-Wu), and a simultaneously voided speciment of urine was sugar-free. A 24-hour specimen of urine gave slight reduction of Benedict's qualitative solution, but showed no oher abnormality. Specimens of urine collected one or two hours after a meal regularly gave slight to moderate reactions for sugar, while fasting specimens were always sugar-free. The reacting substance reduced Nylander's solution, yielded typical osazone crystals with phenylhydrazine, was dextrorotary in the polariscope, was fermented by yeast and was completely destroyed by fermentation.

As a rough test of glucose tolerance, the patient was given 30.0 gm. glucose (about 3.0 gm. per kg. of body weight) in 200 c.c. water, with the juice of one lemon. One hours later, the venous blood sugar was 167 milligrams per cent; 32 c.c. of simultaneously voided urine contained 0.2 per cent of reducing substance by Benedict's quantitative method. This reducing substance displayed the same characteristics as that present in postprandial urine specimens, proving the substance to be glucose.

We wished to determine the patient's calcium and phosphorus balance, but were prevented from doing so by an inadequate period of observation and the patient's capricious appetite. Consequently, during a four-day period of unrestricted general diet, total specimens of urine and stool were collected. The average calcium excretion in the urine was 43.7 milligrams, and in the stool 780.5 milligrams. The average daily excretion of phosphorus was 287.7 milligrams in the urine and 376.0 milligrams in the stool. Determinations were made upon material ashed in a platinum crucible; the technic of the determinations is noted above.

A roentgenological survey of the bony skeleton was made at the Albert Steiner Clinic. The skull is rather round, with a bulging frontal and occipital area. The fronto-parietal suture is closed, while the occipito-parietal is still open. The skull bones are unusually thin, the head having the appearance of the hydrocephalic type. Dentition appears to be progressing normally. The frontal sinuses are not developed as yet. Mastoid cells are just beginning to appear. Sella is normal in size nd shape. The chest is short and broad. The mediastinum is wide. The rib interspaces are narrow. Rib angles are acute. The diaphragms are higher than normal. The cervical, thoracic and lumbar vertrebrae are narrow, giving the impression of being compressed. The head rests nearly on the shoulders. The body is short. The long bones of upper and lower extremities are not well developed in breadth. Their length is apparently normal, but the bones themselves are long and spindling. The epiphyses appear to be developing normally. The texture of the long bones is that of an atrophic or decalcified type. The cortex is unusually thin; the medulla is wider than normal. Both femurs are bowed outward; the tibias are bowed inward, due to muscle pull. The right femur presents a deformity due to

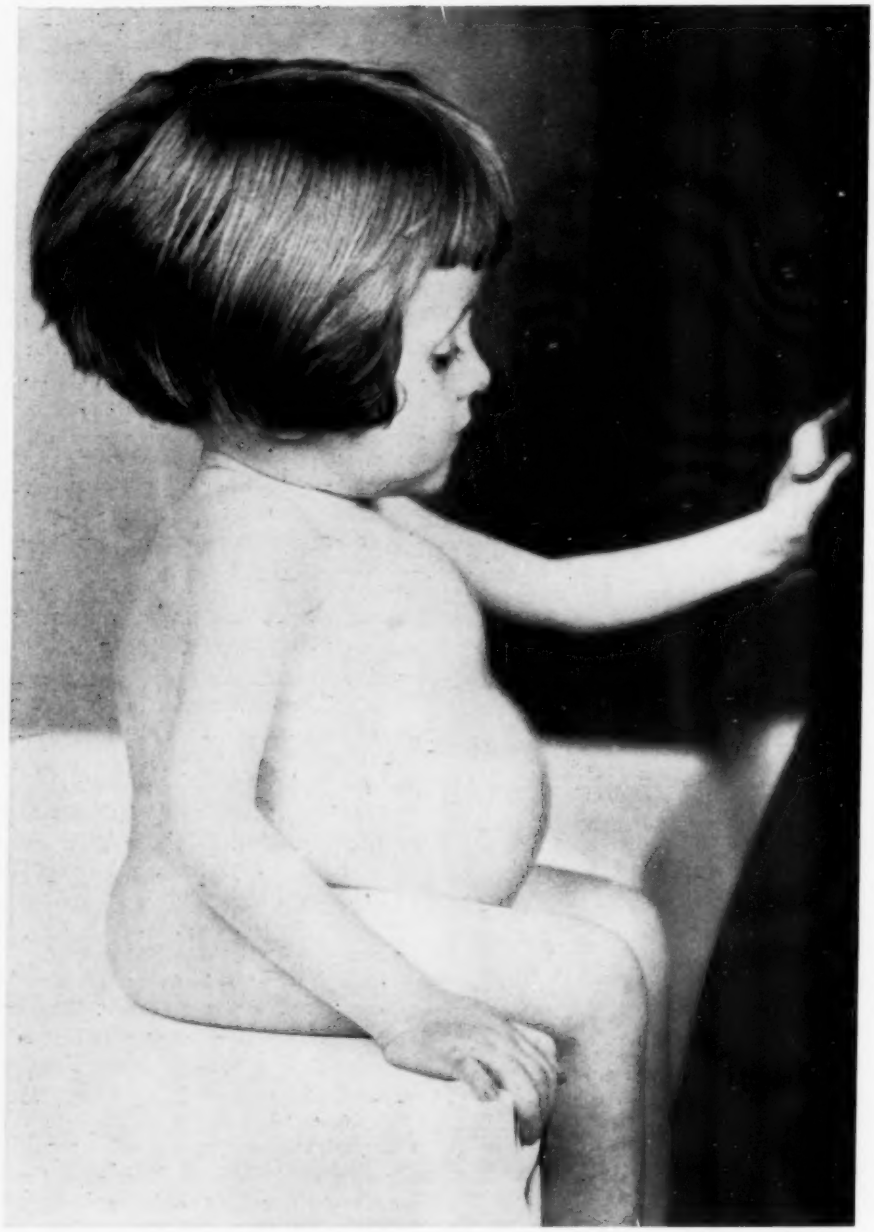

FIG. 1. Side view of patient, showing large head, very short neck, deep antero-posterior diameter of chest, kyphosis of spine, protuberant abdomen, atrophic musculature of extremities.

FIG 2. X-ray showing femurs, tibias and fibulas. The convex light area at the top of the figure is produced by the patient's abdomen.

multiple fractures followed by union and irregular new bone formation. The shaft of this femur has a rather cystic appearance, with marked trabeculation throughout. The ends of all long bones appear expanded, due to the lack of development of the shafts. The pelvis is greatly deformed, pressure from the femurs having pushed the internal surfaces of the acetabular parts nearly in apposition. This giving way of the pelvis has occurred at the lines of epiphyseal union between the lower half and the ileum. There is more atrophy of disuse in the thigh and leg bones than there is in the forearm and arm. None of these bones have the appearance of rickets, scurvy, or syphilis. The carpals and tarsals are poorly developed, as are the phalanges, metacarpals and metatarsals.

Discussion

The excretion of glucose has not been noted in other cases of brittle bones and blue sclerae. In our patient it probably represents a coincidental anomaly. Our investigation was necessarily too incomplete for an exact explanation of the mechanism of the glycosuria. However, it may reasonably be assumed in the presence of a normal fasting blood sugar and a normal blood sugar rise one hour after a relatively large dose of glucose, and in the absence of any clinical symptoms of diabetes, that the glucose excretion represents a benign condition, probably the result of a low renal threshold.

Estimations of chemical constituents of the blood have been made in only a few instances. In Key's patient, the hydrogen ion concentration of the blood was pH 7.58., the serum calcium was 12.17 milligrams per cent, and the blood phosphorus was 4.06 milligrams per cent. In three of Paal's cases the serum calcium readings were 9.06, 9.99, and 12.8 milligrams per cent, respectively. Including the observations in our case, one may say that the serum calcium may be normal or slightly elevated, while the blood phosphorus is practically normal.

Calcium, phosphorus and nitrogen balance studies have been carried out in a few cases of osteogenesis imperfecta; the results of these studies have not displayed a constant abnormality. So far as we are aware, no studies of this type have been undertaken on patients with brittle bones and blue sclerae, except by Key. The balances of his patient were determined in two six-day periods, but the results were never published. In our case, the estimations of the distribution of calcium and phosphorus in the urine and stools showed a greater percentage of both constituents in the stool than is normal. The relative proportions of calcium and phosphorus in the stool were almost the same as in calcium phosphate, which suggests the possible formation of an insoluble calcium compound which cannot be absorbed from the bowel.

The blue color of the sclerae is explained by the majority of authors as an abnormal transparency of the sclerotic coat of the eye which permits the blue uvea to show through. Histologic examination of the affected eye was made in one of Bronson's patients. Other anomalies of the eye have been noted, particularly the presence of embryotoxon in both hereditary and sporadic cases.

The acuity of hearing was normal in our patient. Authorities agree that deafness first appears in early adult life, or later.

The physical characteristics of af-

fected individuals vary, as noted in the descriptions of different authors. The patients are usually small and slender, but two of Key's cases were somewhat obese. The head may be normal in size and shape or show fronto-occipital elongation or an exaggeration of the shape noted in rickets. The fontanelles may remain open for years. There is often deformity of thorax and spine and there may be bowing of the extremities.

Roentgenographic examination of the skeleton displays changes in the skull, the vertebrae and long bones. The sites of previous fractures may show much or little callus. The cortex of the bones may be quite dense, while other portions of the bones cast very faint shadows. Key discusses these changes in detail.

Key gives the only gross and histologic description of excised bone. Hein reports an autopsy on his patient who had multiple fractures at birth, and died of pneumonia at five months of age. The examination revealed fractures of the bones of the skull. No histologic report of the bones is presented.

Nearly all authors call attention to the fact that while fractures result from the slightest trauma, they are usually painless, repair very rapidly, and often leave no deformity.

There is general agreement that the anomaly of brittle bones and blue sclera is due to a hereditary hypoplasia of the mesenchyme.

Treatment can be empirical only in a condition which is so poorly understood. Sunlight, a balanced nourishing diet with sufficient fresh milk to yield an adequate calcium and phosphorus intake, cod liver oil preparations, and ultra violet radiations, constitute rational hygienic therapy. In addition, our case is consuming a quantity of lactose each day, in the hope that it may promote the absorption of calcium and phosphorus from the intestinal tract by virtue of its acid producing effect. Orthopedic procedures are often indicated. Affected individuals may die from intercurrent infection. As puberty and young adult age is reached there is often spontaneous improvement with a greatly reduced liability to fracture.

Summary

A sporadic case of brittle bones and blue sclerae is reported. The clinical picture conforms to cases previously described. In addition, an apparently benign glycosuria is present. Serum calcium determinations gave figures at the upper limits of normal, or slightly above. Estimations of urine and stool calcium and phosphorus gave evidence of abnormally high percentages of both in the stool, in such proportions as to suggest the possibility of faulty absorption from the intestinal tract.

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Argyll-Robertson Pupils In Polyneuritis. Report Of A Case And Theoretical Deductions*

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A CASE in which Argyll-Robertson pupils developed in the course of a toxic polyneuritis and disappeared with the subsidence of the disease should be recorded for two reasons: 1, clinically their presence in such a case leads to a wrong diagnosis, and 2, their occurrence as a part of polyneuritis throws light on their pathogenesis.

A man suffering from chronic cardiovascular-renal disease and chronic pyelonephrosis suffered in six months two attacks of polyneuritis in the second of which his case was studied. Shortly after the onset of the disease, he developed bilateral optic neuritis, Argyll-Robertson pupils, bilateral facial paralysis, signs of meningeal irritation (globulin in the spinal fluid), and signs of central neuritis (spinal cord symptoms). After nine days, the pupils became entirely normal.

In a recent valuable paper, Sven Ingvar[1] reviews in detail the anatomy of the region concerned in the afferent arc of the reflex governing pupillary mobility and discusses the most important causes of the Argyll-Robertson phenomenon.

The afferent pupillo-motor fibers arise in the retina and are most strongly concentrated at the macula lutea. In the optic nerve, chiasm, and optic tract the fibers are superficially placed; in the tract they lie in their respective fields of vision. At the level of the lateral geniculate bodies, the pupillomotor fibers leave the tract, converge, running medially through the brachia of the corpora quadrigemina anterior. Some fibers enter this body, but a compact bundle runs into the dorsal part of the posterior commissure in which it crosses to the other side. It then runs in the descending part of the posterior commissure ventrally to the oculomotor nucleus. Throughout their course in the posterior part of the optic tract and over the superior colliculus, the fibers are extremely superficially placed.

As the case to be presented was free from syphilis, we are interested in all possible causes of Argyll-Robertson pupils. In enumerating the "most important" causes, Ingvar names: 1, syphilitic processes; 2, disseminated sclerosis; 3, polioencephalitis superior of Wernicke 4, epidemic encephalitis; 5, severe chronic alcoholism 6, diabetes

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mellitus; 7, sulphide poisoning; 8, severe traumatism of the skull, and 9, tumors and pathological processes in the region of the anterior corpora quadrigemina. Fuchs[2] states that 10, lead poisoning, and 11, tobacco poisoning may cause reflex immobility, while Moore[3] describes the condition as an occasional 12, congenital manifestation. He also states that Argyll-Robertson pupils may occur as a result of 13, syringobulbia. He quotes Kinnier Wilson as ascribing the condition to 14, diffuse toxi-infective states. We have seen a case (reported elsewhere[4]) in which 15, no cause could be determined and which progressed through the Argyll-Robertson stage to complete ophthalmoplegia interna, but with development of pupillary contraction whenever the patient swallowed anything.

While theories concerning reflex immobility of the pupils are numerous, all heretofore have failed to explain every phase of the phenomenon, and all have failed to explain every case on record. The demonstration of Ingvar, however, seems quite convincing and the occurrence of Argyll-Robertson pupils in the present case, (apparently a unique one), is in entire harmony with this latest account of the pathology of reflex immobility.

Ingvar agrees with Kinnier Wilson[5] and others that the lesion is in the afferent side of the reflex arc. Wilson states that the lesion may be anywhere along this arc up to the synapse of the pupillo-motor reflex fibers with the pupillo-constrictor center in the third nerve nucleus or its vicinity. But Ingvar is more specific in defining the pathology as a marginal destruction within the basal subarachnoidal spaces of the brain. The pupillo-motor fibers have already been followed through this very area (optic nerves, chiasm, optic tract, superior corpora quadrigeminus). He says, "We have to look for the pupillo-motor pathways on the surface of the diencephalon. We know for certain that they take a surface route from the posterior part of the optic tract to the anterior (posterior) commissure in front of the anterior quadrigeminal bodies. As the metaluetic and luetic meningitic processes produce successively developing marginal degenerations of the optic pathways as also of the diencephalic parts on the whole, the pupillo-motor pathways must be injured at an early stage. . . . . The reflex immobility of the pupil is to be considered simply as a meningitis symptom. . . . . As all the evidence indicates that *only such morbid processes as manifest themselves in producing marginal destructions within the basal subarachnoid spaces of the brain are able to cause the Argyll-Robertson pupil,* (the italics are ours), we understand that the metaluetic and luetic diseases hold a monopoly among the causes of this valuable clinical symptom." The case here presented, while apparently unique as an occurrence, nevertheless is easily understood on the basis of the above pathology and thus corroborates the interpretation of Ingvar.

Report of the Case

A man of 62 years, whose family history was not noteworthy, came complaining of pain and weakness in the legs. Of childhood disease, he had

had only diphtheria which had left him with weakened muscles of the throat. Aside from this, he had had no serious illness until he suffered an attack of appendicitis in 1924, following which he had developed a colon bacillus cystitis and bilateral pyelitis.

In the summer of 1928, he had experienced no urinary trouble for over a year, when he suddenly developed pains and stiffness in the arms followed by a marked weakness. This progressed until he was unable to comb his hair or raise even a cup to his lips. After some weeks he recovered. (During his illness he was examined by Drs. Crane and Jackson of Kalamazoo, Mich., whose complete records were kindly placed at our disposal and which show definitely that the patient's pupillary reflexes were entirely normal prior to his consulting the present writers.)

March 15, 1929, the patient developed severe pains in his legs followed by weakness. This progressed until he was able to stand only if his knees were set straight, but if they bent he would sink to the ground. On the tenth day, he developed suddenly a paralysis of both sides of his face, and four days later he came under the care of one of us. In the general examination, the findings worthy of note were: Blood pressure 180-220 systolic, 100-110 diastolic, widening and tortuosity of the aorta (seen by fluoroscope), heart dulness 11 cm. to the left and 3 c.m. to the right of midline, second aortic accentuated, brachial and radial arteries definitely thickened on palpation, much pus in urine, and a trace of sugar in three specimens, none in two others, blood Wasserman negative, N.P.N. 37.8, uric acid 3.6, sugar 150 mg. per 100 c.c. of blood, red cells 5,020,000, white cells 8,400, of which polymorphonuclears made up 65% and small mononuclears 35%. The pupils were found to be rigid to light stimulus, but contracted well on convergence. There was a bilateral facial nerve paralysis as shown in Figs. 1 and 2. Abdominal and cremasteric reflexes were absent, sensation was disturbed in the lower extremities below the knees. There was marked weakness as described above.

A neurological examination presented the following (in abstract): The pupils were unequal, right greater than left. Both responded sluggishly to light, the right possibly not at all. Both responded well on convergence. Hearing, smell and taste were unaffected. There was complete paralysis of all muscles supplied by both facial nerves, as a result of which the palpebral fissures were widened. During downward gaze and attempt to close the eyelids, these moved up slightly. During upward gaze, eyeballs and eyelids were both up above the normal (hyperkinetic symptoms due to overaction of unopposed muscles). Pressure pain was diminished on both sides. There was no paralysis of any muscles of the lips or mouth and deglutition was normal. The hand grip registered 70 right and 80 left on the dynamometer. No paresthesias, anesthesias or pains in the arms or hands were found. Abdominal reflexes were absent. All movements of the lower extremities were weakened. Patient could stand if knees were stiffened. All reflexes (superficial and deep) in the lower extremities were absent. There was no

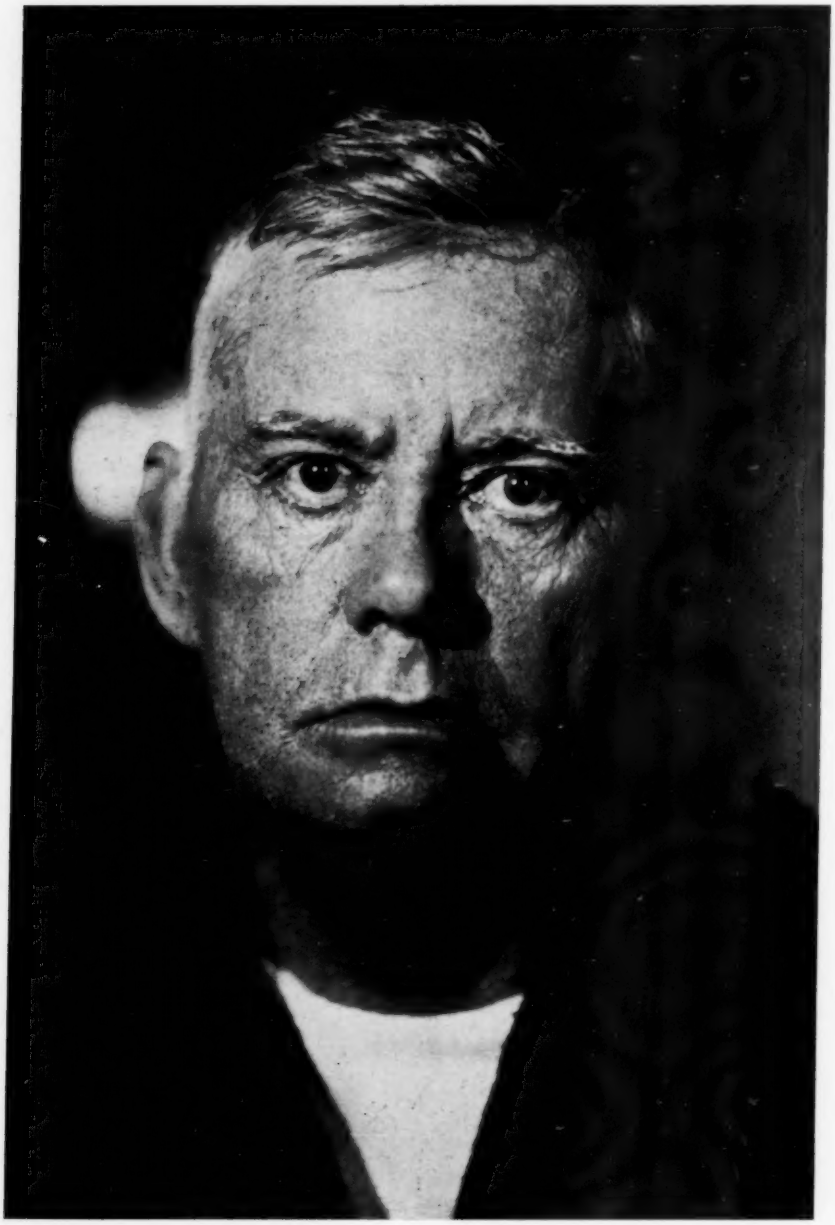

FIG. 1. Argyll-Robertson pupils in polyneuritis.

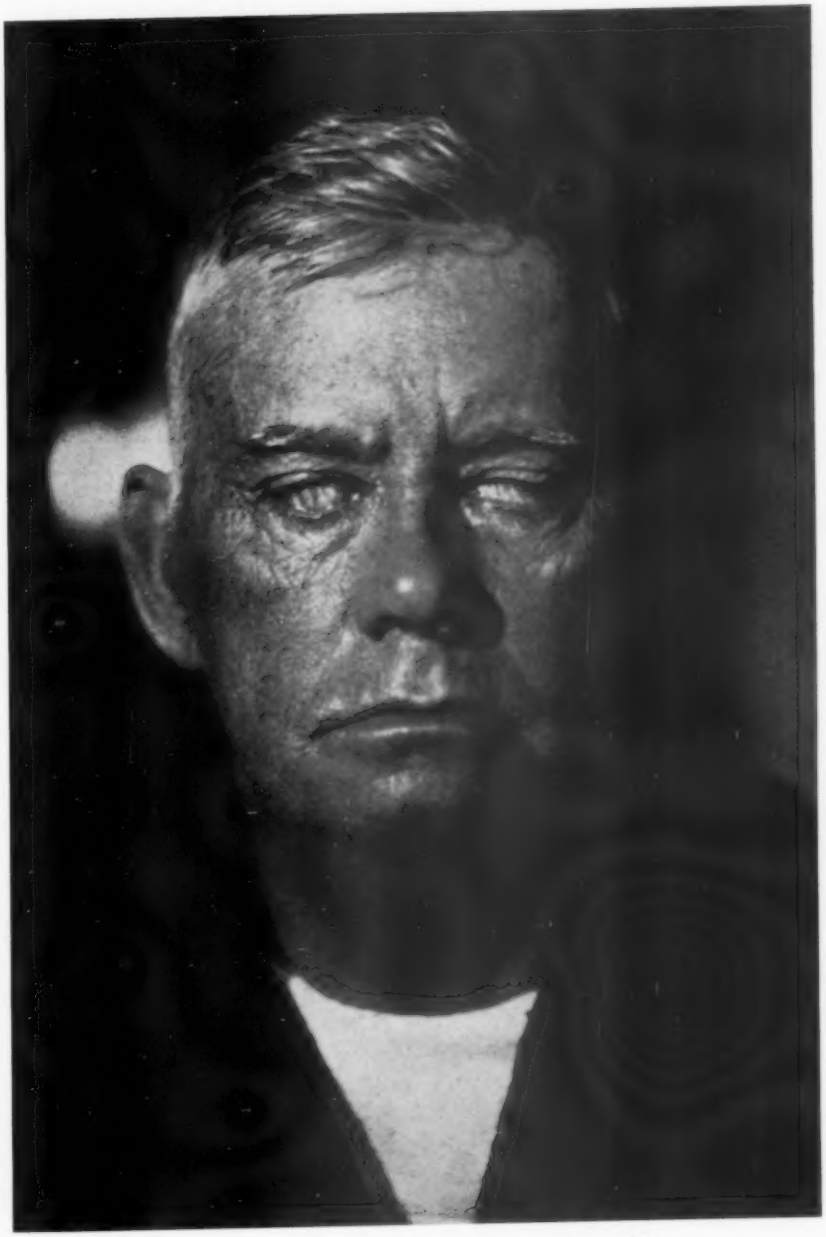

FIG. 2. Argyll-Robertson pupils in polyneuritis.

tenderness along the nerve trunks and no anesthesias or paresthesias, but considerable pain was present in the lower extremities.

Four days later an examination showed that the pupils had become completely fixed to the light reflex. The right was 5 mm., the left 4 mm., both irregular in outline. In addition the arms and hands had become painful and considerably weaker. On the other hand, the right Achilles reflex had returned. There was an absence of vibration sense on the right up to the level of the tenth dorsal segment. On the left this extended only to the third lumbar segment.

Still five days later a re-examination was made, and the striking fact discovered that the pupils responded very readily to light. They were equal in size, regular in outline, and showed no abnormality of any kind. The facial nerves were still completely paralyzed. The arms and hands had become tender, much weaker (R. 45, L. 35) and an area of hypesthesia had appeared along the ulnar surface of the left hand. A zone had appeared at about the 8th dorsal segment below which sensation to pin prick was diminished and above which it was normal. Another line of demarcation had appeared at about the knee level below which sensation to pin prick was much diminished.

Tests for reaction of degeneration were made on both sides of the face, both forearms and both legs. An incomplete reaction of degeneration was found in all groups tested. The facial nerves were most completely involved, those of the forearm regions next, those of the legs least.

A fundus examination showed a bilateral neuroretinitis, many hemorrhages and exudate near the papillae. There was also a high degree of retinal arteriosclerosis.

A spinal puncture showed 200 mm. water pressure, 3 cells per cu. mm., globulin 4 plus by the Pandy, plus by the ammonium sulphate method, Wassermann test negative, sugar 111 mg. per 100 c.c., Lange colloidal gold curve negative.

From this time no extension of the disease was observed. In two weeks, the patient could walk, a week later upper facial movements began and the eyes closed fairly well. The abdominal reflexes were still absent, but the cremasterics and deep reflexes had returned.

It was obviously important to determine, if possible, whether the optic neuritis was due to the cardiovascular-renal disease or was a part of the general polyneuritis. An examination was made in June, revealing a marked subsidence of the polyneuritis and also of the optic neuritis. The swelling of the nerve heads had decreased from two diopters to one-half diopter and the other manifestations had diminished. There was still considerable involvement of the right facial nerve, little of the left, and considerable weakness remained in the lower extremities. The cardiovascular disease had not diminished. We, therefore, conclude that the optic neuritis came and receded with the general polyneuritis and bore little, if any, relation to the cardiovascular renal syndrome.

Discussion

When the patient was first seen by us, he had Argyll-Robertson pupils. We found it necessary to consider the patient a syphilitic who had developed polyneuritis. It was learned through a great deal of questioning that the patient had worked in composition shingles (exact chemical composition unknown) just prior to each of the two attacks of polyneuritis, and his pyelonephrosis had been peculiarly quiet during this time. When the pupils became normal, we were suddenly faced with the necessity of explaining the pupillary condition as due to polyneuritis, or the two conditions due to one cause. Kinnier Wilson's statement that reflex immobility may occur in the course of acute toxi-infective states would seem to satisfy us clinically, but not pathologically.

From the pathological standpoint, we considered other explanations. That central neuritis occurs quite frequently in polyneuritis is known and has recently been called to our attention again[6]. In the case presented, we were unable to show evidence of central neuritis above the level of the D8 segment. A non-specific central neuritis in the region of the oculomotor nucleus which caused Argyll-Robertson pupils and nothing else would have to be assumed to be as specifically selective pathologically as that assumed by some to occur in such pupils when of syphilitic origin. Such assumptions would be entirely speculative. On the other hand we found a bilateral optic neuritis and considerably increased globulin in the spinal fluid. We, therefore, know without assumption that inflammation of the regions traversed by the afferent pupillo-motor fibers was in progress. With the onset of this inflammation, Argyll-Robertson pupils developed, with its subsidence they disappeared. We feel justified in concluding that the case corroborates entirely Ingvar's explanation of the pathogenesis of reflex immobility of the pupils.

Summary

A case is reported in which during the course of an acute polyneuritis Argyll-Robertson pupils, bilateral optic neuritis, and bilateral Bell's palsy developed. The pupils became normal on the ninth day. Evidence is furnished by the unique case to show that Sven Ingvar's ideas of the pathogenesis of reflex pupillary immobility are probably correct.

The writers are indebted to Dr. W. H. Riley for the first neurological examination and to Dr. L. V. Stegman for the fundus examination.

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Undulant Fever In Man. Report Of A Case Due To Brucella Abortus

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ABOUT twenty-five years ago[1] attention was directed toward the Island of Malta because of the prevalence there of undulant fever.[2] An intensive study proved that goats harbored the disease and that raw goat's milk was capable of transmitting the infection to man.[3]

The infecting organism was identified as Brucella melitensis[4] and the diagnosis of the infection was simplified by the development of serum agglutination tests[5].

The study of Brucella melitensis has not been confined to Malta and adjacent Mediterranean regions but has now embraced grazing areas in every continent. In the United States the disease was found to be common in Texas[6] and human infection not unknown.[7] An epidemic occurred in Albuquerque, N.M., following the importation of goats, and some thirty human cases were recognized within a few weeks.[8] Agglutination tests of the goat's serum have proved that these animals were the source of the disease and it has been shown that the organism can be isolated from the milk.

Today a new situation confronts us. Two other domestic animals have been shown to harbor the Brucella type of organism. A species of Brucella melitensis is found in hogs, and human infection by this porcine type is becoming recognized in increasing numbers. Even more alarming is the incidence of infection in cattle by a similar organism, Brucella abortus. More than two hundred human cases have recently been reported as due to bovine or porcine infection: 125 cases in Iowa,[9] 50 cases in Michigan, and 91 cases in New York.

The differentiation of these species has been made possible largely through the pioneer work of Dr. Forrest Huddleson[10] in Michigan, and that of Dr. Alice Evans[11] who, herself, became infected with the disease.

Three main avenues exist for the transmission of the infection from animals to man:

First, cow's milk has been shown to contain Brucella abortus.[12] The ingestion of raw milk is dangerous.

Second, close contact with infected animals may lead to infection. This is particularly true in abortion and the handling of new-born calves or pigs.

Third, a number of laboratory workers have developed the disease. Huddleson[13] reports three cases among his confreres, and four scientists of the U. S. Public Health Service have contracted undulant fever.

Case Report

The case to be reported is that of a telephone construction engineer, 30 years of age. The patient drank raw cow's milk habitually but used no goat's milk, and did not come in contact with domestic animals. He was referred to me after having been treated for two weeks, the provisional diagnosis being grippe and tuberculosis.

The symptoms were fever, sweating, nervousness, anorexia, afternoon headache, tremor, and cough.

The fever began so gradually that the patient continued to work for the first week. At the end of the second week the temperature reached 102° each afternoon, with a drop to 100° in the morning.

The physical examination was practically normal except for tremor of the fingers and tongue, sweating, fever and exaggerated reflexes.

Urinalysis was negative. Hemoglobin 74%; erythrocytes 5,550,000; leucocytes 6,150; polymorphonuclears 28%; lymphocytes 66%; large mononuclears 4%.

These findings seemed sufficient to exclude tuberculosis, typhoid fever, and rheumatic fever. Undulant fever was suspected, and an agglutination test requested. This was found positive, at about the 18th day of illness, in dilution of 1 to 320. Two weeks later it had increased in titer to 1 to 2,560 (Brucella abortus).

Two blood cultures and two urine cultures were negative.

The course of the fever was atypical. It subsided during the fourth week. For three days the temperature was normal. Then for one week only fever recurred, reaching 105°. The administration of Mulford's Anti-melitensis serum may have hastened the decline. There has been no further recurrence in fifteen months. However, the serum agglutination has remained strongly positive.

The physical signs were also atypical. The spleen was not felt at any time. There was no adenopathy. No arthritis or orchitis occurred and no muscular pains.

Discussion

This is a case of undulant fever due to bovine Brucella abortus apparently contracted from drinking cow's milk. The patient resided in a city of over 150,000 inhabitants, where the milk is carefully inspected. However, no tests are made to determine the presence of Brucella abortus in the milk. Nor are the herds tested to determine the prevalence of infection.

The incidence of infection of cow's milk with Brucella abortus is surprisingly high. One authority estimates that at least 90% of our dairy herds are infected.[14] Presumably even certified milk from such herds would be contaminated. Pasteurization should destroy the organism.

An illuminating chapter in the epidemiology of Brucella abortus was recently written at the Metropolitan Life Insurance Company Sanatorium, at Mount McGregor, N.Y. Patients and staff men were tested for one year for Brucella abortus. Out of 599 sera, 82 gave a positive agglutination. Several infected cows were then removed from the company herd, and for eight months no new patients came down

with Brucella infection. However, after this interval, nine additional patients became infected, and a check-up of the herd showed that another animal had a positive agglutination.[15]

It would seem that we are facing a new public health problem inherent in the dairy and hog-raising industries. In the previous generation notable progress was made by Bruce, Hughes, and others, to control undulant fever due to goat's milk. In our generation Huddleson and Evans have pointed the way to safeguard our milk supply.

The problem is somewhat analogous to that of bovine tuberculosis. The elimination of tuberculin-positive cattle is rapidly becoming an accomplished fact. For Brucella infection a similar campaign of elimination may be feasible.

The danger of transmission from animals to man undoubtedly is much greater than has been realized heretofore. Several fatal cases are already recorded and the morbidity is very great in many cases that recover. With current simplification of the diagnosis many more cases will probably be discovered.

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Medicine And The Muse

Oliver Wendell Holmes, M.D.

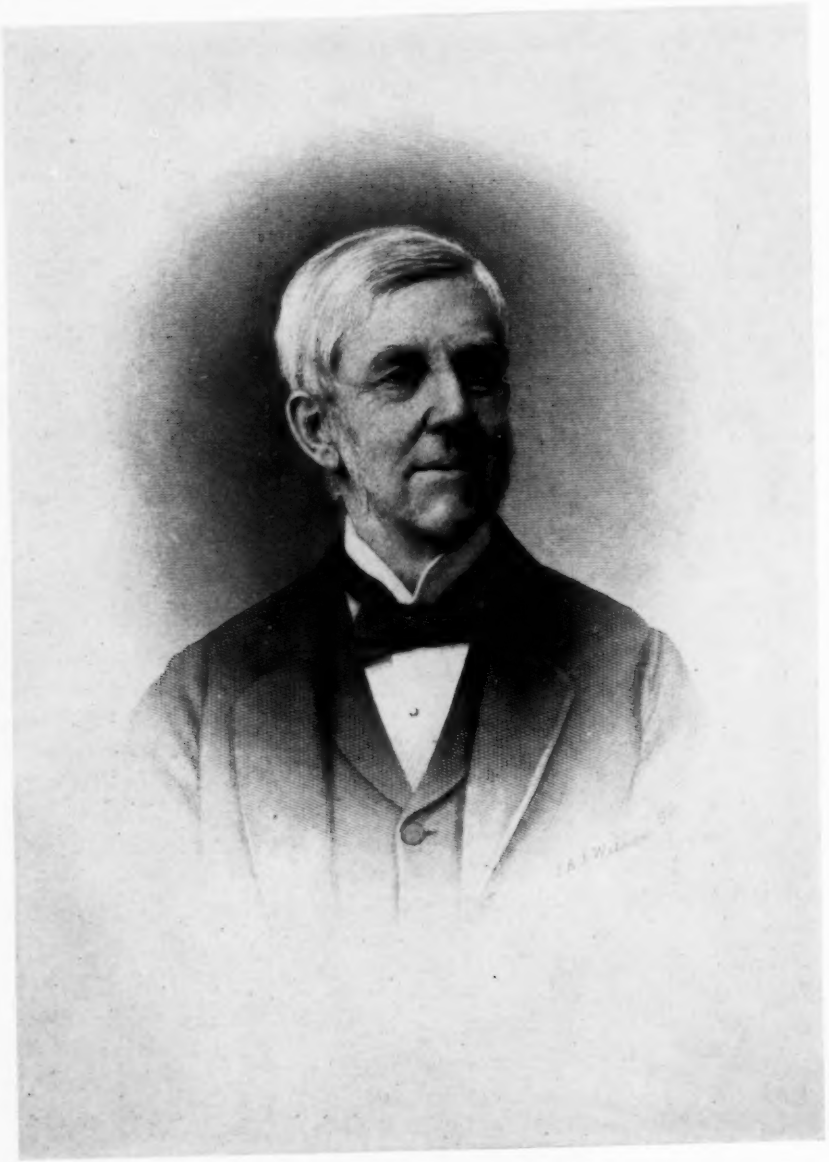
By Lieut.-Comdr. Louis H. Roddis, *Washington, D.C.*

GENTLEMEN: DAMN the sphenoid bone! This was the annual preface to the lecture on the sphenoid given by Dr. Holmes to freshmen medical students at Harvard during their course in osteology. As he was Parkman Professor of Anatomy from 1847 to 1882, a period of thirty-five years, it became a sort of ritual, a kind of annual event at Harvard to which students looked forward. Every physician and student of medicine will know the reason for such profanity in reference to the sphenoid, for with the exception of the temporal bone it is the greatest stumbling block to the medical student in his whole course in osteology. Cunningham's Anatomy gives sixty separate facts it is necessary to learn about this small keystone of the skull. There are sixty-four descriptive facts given about the temporal bone and it is largely a matter of individual taste, or rather distaste, as to which constitutes the worst obstacle to the student. The weight of medical tradition, however, indicates the sphenoid and Dr. Holmes expressed the opinion of many a long-suffering freshman .

Oliver Wendell Holmes was born at Cambridge, Massachusetts, on the 29th of August, 1809. His father was the Reverend Abiel Holmes, a Calvinist preacher. His mother, Sarah Wendell, was a descendant of Governor Simon Bradstreet, distinguished in the early history of the Massachusetts colony. He was at first destined for the law but soon began the study of medicine, a profession in which he was to take a high place as the co-discoverer with Semmelweiss of the method of transmission of puerperal sepsis and its prevention.

It was while a student at Harvard that Holmes leaped to fame as the author of some verses that have been repeated so frequently by American school boys that few productions of an American poet are more universally known. The Navy Department had decided to sell the old frigate Constitution celebrated for her victorious engagements with the British frigate Guerrière, and the sloops Cyane and Levant, as well as for her escape from the British squadron of Sir George Collier. There was much public disapproval of the sale but it was not sufficiently well expressed to deter the Navy Department from going ahead with its disposal. Then there appeared in the Boston Daily Advertiser the stirring lines of "Old Ironsides":

Aye, tear her battered ensign down!
Long has it waved on high,
And many an eye has danced to see



Oliver Wendell Holmes, 1809-1894

That banner in the sky;
Beneath it rung the battle's shout,
And burst the cannon's roar;—
The meteor of the ocean air
Shall sweep the clouds no more!

This poem was reprinted everywhere and the wave of enthusiasm it caused so crystallized public sentiment that it led to the rescinding of the order to sell the old vessel.

In 1833 young Holmes went to France to continue his medical studies. That country then held the place now occupied by Germany as a center of medical research and the names of Louis, Laennec, Broussais, Corvisart, Larrey, Dupuytren, and Velpeau gave the prestige to French medicine that in our day is conferred on Germany by those of Koch, Klebs, Löffler, Ehrlich, von Behring, Billroth, and von Esmarch.

In 1835 Holmes returned to Boston and began practice. During this period from 1835 to 1845 the valuable observations in reference to puerperal sepsis were made that form his principal contribution to medical progress and which give him a noteworthy place in the history of American medicine. Childbed fever was then like smallpox before vaccination a dreaded disease, the cause and mode of transmission of which were unknown.

In 1843 in the New England Quarterly Journal of Medicine Holmes published an article, "The Contagiousness of Puerperal Fever," and in it he boldly and plainly stated that puerperal sepsis was contagious and doctors and nurses the principal carriers of the infection. This statement was supported by the strongest sort of evidence. He gave a careful summary of the observations that led to this conclusion. His recommendations for prevention were so simple and yet so correct that had they been adopted they would have at once resulted in a tremendous reduction in maternal mortality. The essay is rightly considered one of the classic documents in medical literature and should be read by every physician, not only because it contains the original announcement of an epoch-making observation that has led to the saving of millions of lives and the prevention of an enormous amount of human suffering, but as an example of clear and logical reasoning and of a fine yet restrained literary style. Not the least important part of Holmes' paper was the generous credit he gave to earlier students of the subject. This is particularly true of Charles White of Manchester to whose pioneer work he makes frequent reference. The bibliography at the end of the article also furnished a very complete review of the literature of puerperal fever.

Holmes met with the most bitter opposition from the leading obstetricians of the day and the weight of their influence effectually prevented any general adoption into practice of his views. However, in 1847 Semmelweiss announced from the clinic of the Allgemeines Krankenhaus in Vienna that puerperal sepsis was due to absorption into the blood from the genitals of decomposed animal matter and that the hands or any article brought into contact with the genitals of the parturient, might be carriers of the contagion. By simple measures he reduced the mortality of the lying-in-wards of the

Krankenhaus from 11.4 per cent to 1.27 per cent. It is of interest to compare the recommendations of Holmes and Semmelweiss:

Holmes	Semmelweiss
1. A physician holding himself in readiness to attend cases of midwifery should never take any active part in the post mortem examination of puerperal fever cases.	1. Thorough washing of the hands with soap and hot water.
2. A physician present at such post mortems should use thorough ablution, change every article of dress, and allow twenty-four hours or more to elapse before attending a case of midwifery.	2. Cleaning of the finger nails.
3. Similar precautions should be taken after the autopsy or surgical treatment of cases of erysipelas if the doctor is obliged to unite such duties with his obstetrical work, which is in the highest degree inexpedient.	3. Immersing the hands into a solution of chlorin water (later he recommended a chlorid of lime solution).

Both Holmes and Semmelweiss were directed to the inquiry of the subject by similar circumstances. Holmes was struck by the frequency of post mortem sepsis in the practice of physicians after they had been performing autopsies. Semmelweiss was present at the autopsy performed on his friend and demonstrator of anatomy, Professor Kolletschka, who died from an infection following the pricking of his finger while performing a post mortem. He observed the similarity of the finding in Kolletschka's body and in those of women who had died of puerperal fever. Semmelweiss met with opposition of a more violent character even than had Holmes and the remainder of his life was devoted to controversy and struggles for the general adoption of the methods of prevention he had put into practice at the Vienna Allgemeines Krankenhaus. The fight was a long and bitter one and ended only with the death of Semmelweiss and though he did not receive recognition during his life time he was scarcely dead when his work was accepted and with the advent of Lister, Pasteur, and Koch its true worth was revealed.

Semmelweiss deservedly holds the highest place in the history of the conquest of childbed fever, but Holmes will not be forgotten as the greatest of the pioneers in the field, for the generous credit he gave to previous workers, and the classic excellence of the essay in which his results were given to the world. Both Holmes and Semmelweiss possessed the high moral courage required of the heretic and the rebel in stating their convictions. Child-bearing women of every land and time owe a great debt of gratitude to both of these men, and womanhood everywhere would honor itself with tributes to their memories.

In 1856 Holmes began the publication in a series of essays under the title of the "Autocrat of the Breakfast Table." Their success was such that the Professor at the Breakfast Table and the Poet at the Breakfast Table followed. From the beginning of the Autocrat, Holmes devoted himself more and more to literature and soon gave up the active practice of medicine. He was however in 1847 ap-

pointed Parkman Professor of Anatomy at Harvard and his work there kept him in close contact with his profession. His lectures were looked upon by the students as oases in an educational desert and this despite the fact that anatomy is commonly regarded as a rather dry subject. As seen by the opening sentence to his lecture on the sphenoid bone, his methods of instruction were such as to command attention. It is said that his classes were held toward the close of the day as he was the professor who could best hold the interest of tired students. Whether this was true or not, his lectures were long remembered with pleasure by those who attended them and many are the anecdotes recorded and unrecorded of the lecturer and his instructions.

Holmes' fame as an essayist was established by the Autocrat, but it is not so well known that his medical essays are of equally high quality and that most of them may be read with pleasure by the laymen as well as the physician. In addition to the essay on puerperal fever which was reprinted by him in 1855, they include a delightful essay on Homeopathy and its Kindred Delusions, Border Lines of Knowledge in some Provinces of Medical Science, Currents and Counter Currents in Medical Science, Scholastic and Bedside Teaching, The Young Practitioner and Medical Libraries. Two essays, The Medical Profession in Massachusetts, and Some of My Early Teachers, are valuable contributions to medical history. A little known though interesting sketch is a lengthy introduction by Holmes to a little book called Visions, A Study of False Sight (Pseudopia) by E. H. Clarke, published in Boston in 1878.

The humor that distinguishes the essays is found throughout the poetry. The verses telling of the effect of this humor on a servant is a characteristic piece of writing:

He took the paper, and I watched,
And saw him peep within
At the first line he read, his face
Was all upon the grin.

He read the next; the grin grew broad,
And shot from ear to ear;
He read the third; a chuckling noise
I now began to hear.

The fourth; he broke into a roar;
The fifth; his waist band split;
The sixth; he burst five buttons off,
And tumbled in a fit.

Ten days and nights, with sleepless eye,
I watched that wretched man,
And since, I never dare to write
As funny as I can.

Holmes was in great demand at class reunions, alumni association dinners, at the entertainment of visiting notables and indeed all sorts of public social affairs. His invariable contribution was a poem and some of his happiest efforts were for these occasions. This stanza for a Harvard alumni reunion in 1857 is an example:

What dreams we've had of deathless name,
  As scholars, statesmen, bards,
While Fame, the lady with the trump, held up
  His picture cards!
Till, having nearly played our game, she gayly
  Whispered, Ah!
I said you should be something grand,—
  You'll soon be grandpapa.

More serious, yet in a playful mood too, is "The Boys" for the Harvard reunion of 1859. The gray haired men gathered there preserve the illusion that they are still the youngsters of the old days on Harvard's famous campus:

We've a trick, we young fellows, you may have been told,
Of talking (in public) as if we were old:
That boy we call "Doctor", and this we call "Judge";
It's a neat little fiction,—of course it's all fudge.
That fellow's the "Speaker"—the one on the right;
"Mr. Mayor", my young one, how are you tonight?
That's our "Member of Congress", we say when we chaff;
That's the "Reverend" what's his name?—don't make me laugh.

And the fine concluding lines:

Then here's to our boyhood, its gold and its gray!
The stars of its winter, the dews of its May!
And when we have done with our life-lasting toys
Dear Father, take care of thy children, THE BOYS!

Here are the opening lines to verses read at what must have been a more convivial dinner, that given for Admiral Farragut July 6, 1865:

Now, smiling friends and shipmates all,
Since half our battle's won,
A broadside for our admiral!
Load every crystal gun!
Stand ready till I give the word,—
You won't have time to tire,—
And when that glorious name is heard,
Then hip! hurrah! and fire!

His fame as a poet, of course, does not rest on this relatively light and fugitive verse but on such splendid pieces as Old Ironsides, The Battle of Bunker Hill, The Wonderful One Hoss Shay and the Chambered Nautilus, the latter one of the best known and most widely quoted poems in the English language.

Dr. Holmes wrote the most extensive collection of what may be called "medical poems" in the language. There are more than twenty devoted to themes in which only a physician would show interest and containing the medical terms suitable to the subject. There are The Stethoscope Song, Extracts from a Medical Poem, Rip Van Winkle, M.D., Meeting of the National Sanitary Commission and verses on Joseph Warren, M.D., the physician patriot whose death at Bunker Hill was so great a loss to the cause of the colonists. There is a poem in honor of Keats, also a physician, and a fine eulogy to the medical profession is contained in verses read at the Centennial Anniversary Dinner of the Massachusetts Medical Society June 8, 1881. There are some unmistakable expressions in the One Hoss Shay that inform us that the author was a doctor.

Many physicians have abandoned medicine for letters and as Sir William Osler has pointed out, many physicians have attained fame as men of letters but they have done so at the expense of opportunities for distinction in their profession. Holmes is the only exception. In him we have one who was famous in both fields, medicine and literature, and in the latter a master of two mediums, poetry and prose.

Dr. Holmes was a notable member of the famous Saturday Club of Boston where Longfellow, Whittier, Emerson, Lowell, Sumner, Motley, Parkman and Agassiz were accustomed to gather. Among them all he was regarded as the best conversationalist. He talked even better than he wrote. Throughout his long and active life he was a leading figure in Boston's social literary and professional circles. He took no part in politics though he was an ardent abolitionist. His eldest son, now a member of the United States Supreme Court, served as an officer in the Union Army.

In 1886 he made a journey of four months in Europe where he was received everywhere with pleasure and respect. The degree of Doctor of Letters was conferred upon him by Cambridge University, Oxford made him a Doctor of Civil Law, and Edinburgh University a Doctor of Laws.

After his return he wrote "One Hundred Days in Europe" in which he reviews the kindness, the hospitality and the praise he received there. In 1888 appeared the series of charming papers known as "Over the Teacups" and in 1889 the poem for his Harvard class reunion, "After the Curfew," distinguished for its pathos and its expression of noble hope. These three productions are remarkable as the work of a man of four score years, and show what accomplishments are still possible to a serene and splendid old age.

Dr. Holmes died October 7, 1894, and is buried in Mount Auburn Cemetery.

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Editorials

THE MINNEAPOLIS CLINICAL WEEK.

Another year has come around, and the necessary plans are now being made for the Annual Clinical Meeting of the College, which is to be held this year in Minneapolis during the week of February tenth. The Minneapolis men have chosen this season, the coldest of their Winter, in order to demonstrate how comfortable they can make it for their visitors. They promise a clear, dry, cold atmosphere, sparkling snow and brilliant sunshine, with Winter sports in great variety as external attractions; while internally there will be perfectly heated and ventilated rooms, with that degree of comfort which only the inhabitants of the Northwest know how to provide against the rigors of their climate. Long experience has perfected in them the art of adapting life perfectly to their long and cold Winters; and the visitor from warmer climates may be assured that this clinical session will be carried out under conditions even more comfortable than would be the case in warmer climes where the art and science of living warmly are less well developed. The attractions of Minneapolis as a city are many and varied; and it will be especially interesting to see it in the depth of its Winter season. The location of the twin cities upon the banks of the winding precipitous gorge of the Mississippi, the frozen river, lakes and waterfalls, bordered by snowy forests, all offer a scenic setting of the greatest interest. The imagination is intrigued by the fact that the two cities of Minneapolis and St. Paul, so closely connected as to seem but one, are in reality the Gateway to the Great Northwest, the land of wheat, the endless plain of Minnesota and the Dakotas, stretching illimitably into Manitoba and the frozen North. When one stops to think of the youth of the land, barely a generation from the Indian, the immigrant wagon and the homesteader, amazement must fill the mind at the wonderful growth and development of this region in the last fifty years. The giant grain elevators and flour mills speak eloquently of the chief causes of that development, and the source of the wealth so evident in the buildings and homes of the two cities. The University and the Art Galleries of Minneapolis speak also for the development of intellectual culture which has paralleled that of the material prosperity of the city. And its medical development has been as amazing, as one will see from the article and illustrations by Dr. Marx White in this issue, in which are described and shown the numerous capacious and up-to-date hospitals of the community. To these medical facilities furnished by various social factors and agencies the University Medical

School must be the pivotal center around which all revolve, and from which all receive helpful stimuli. Here in the school and in the outlying hospitals and clinics a wonderful postgraduate week of clinical instruction and demonstration is being arranged for the Clinical Week. It is hoped that this wonderful opportunity, which is prepared for the Fellows and Associates of the College, will be made use of by a goodly representation; and that this meeting will pass into the history of the College as one of its best and largest. Therefore, each Fellow and Associate is urged to plan now to come to Minneapolis in February. A break in professional work in this month is highly desirable; an instructive vacation of a week in postgraduate work cannot fail to be most highly stimulating and profitable; and he who attends will go back to his work freshened in mind and spirit, and with a new zest. Not the least of all the advantages of Clinical Week is the opportunity it offers for the renewing of social relations among the members of the College. This after all is one of the chief functions of the annual meeting. The College is acquiring a distinguished personnel in its membership—it is good for these members to come together, to know one another personally and to establish bonds of intimacy and friendship. Through such the ideals of internal medicine for which the College stands can be brought closer to realization.

SENSATIONAL SCIENCE.

The recent widely heralded alleged discovery in the public press of the etiological agent of influenza leaves an unpleasant taste in one's mouth. In the first place the manner of announcement discredits the achievement, whatever that may be. The proper place for the report of such a discovery is through the pages of a scientific journal, or through the medium of a scientific society directly interested in the branch of science concerned. But when an alleged scientific discovery is given out through the columns of a daily paper, then, at once, one is justly suspicious that desire for public notoriety, rather than scientific zeal, lies at the bottom of the announcement. Modern sensational journalism has invaded the sacred precincts of the investigating laboratory. Medical research of a certain kind has taken on a news value, and the reporter haunts the doors of science as he does those of the police station or of Congress. He applies the same criteria of sensationalism to the material he selects for publication from all of these sources. What has public interest is only that which will cause a cheaply sensational momentary thrill of interest in the minds of the readers, the majority of whom read only the head-lines. In the truly scientific accomplishment the journalist has no interest, and scores of splendid contributions to medical knowledge are passed unnoticed, because they lack such news value. But a cancer cure, a cause for cancer, the cause of influenza, and the like, offer possibilities for tickling the fleeting interest of the average reader, and hence have what is popularly called a news value. Wholly regardless of the futile hopes exalted in the breasts of thousands of cancer victims the newspapers will callously publish, almost from

day to day, accounts of the discovery of new cancer cures, which soon pass into oblivion and are forgotten by all except the friends of the victims whose hopes were so cruelly excited only to be blasted. The newspaper records of the International Congress of Physiology, held in Boston last August, are very revealing. Take the leading New York dailies, for instance, they suffer from the very same type of journalism. Of all the worthy and truly scientific matter presented at that Congress there was practically no notice taken, but columns appeared relating to various psendoscientific accounts of cancer and rejuvenation presented at the meetings. In this respect the papers assume the value of a fake teacher and a false prophet in the choice and dissemination of such news material. The worst aspect of the whole situation is its reaction upon certain scientific men and research institutions; they actually came to encourage the premature publication of scientific investigations, or to give to their work an assumed importance which scientifically it does not possess. Even a suspicion of intentional dishonesty attaches itself to some newspaper performances of this kind. If not that, certainly the poorest possible judgment and questionable taste. In a popular journal devoted to the home there appeared recently a sensational article on Undulant Fever stating that thousands of cases of this disease were due to milk drinking, when as a matter of fact the Public Health Reports list less than a thousand cases all together. Not always, however, is the scientist, himself, to blame for the situation in which he may find himself. The reporter may twist and exaggerate, select words or phrases without context, and give to the reader an entirely wrong conception of an honest piece of work. Even with the greatest care an honest and modest worker may be caught. The attempt to control the situation by the development of special news agencies, such as Science Service, is subject to the same criticism, because of the choice of news exercised, the same false conception of material used. The harmfulness of the situation can be easily seen if one looks back through the daily papers of the last ten years and notes the so-called great medical discoveries that have held first place, with head lines, in their columns. Where are they now, these great discoveries? Where is the Gye-Barnard cause of cancer, the cancer bacillus, the Blair Bell lead treatment, the Noguchi cause of Yellow Fever, the Voronoff and Steinach methods of rejuvenation, and a dozen others? In the same limbo to which will be presently consigned the Gerson diet-cure for tuberculosis, the Calmette method of immunization, the Pearl treatment of cancer with tuberculin, and, most probably, the recent discovery of the cause of influenza. It is unforunate that the public interest in medical matters cannot be more intelligently directed, so that medical discoveries will be accorded their real value, and no false hopes excited. Surely there are definite moral principles involved in this giving out and the publication of the results of medical research.

Abstracts

A Study of the Pellagra-Preventive Action of Canned Salmon. By JOSEPH GOLDBERGER and G. A. WHEELER (Public Health Reports, Nov. 15, 1929).

A test of the black tongue-preventive action in the dog of canned salmon showed that it had a decided preventive action, resulting in full protection against this condition. In view of the abundant evidence that canine black tongue is the analogue of human pellagra, a comparable study of the value of canned salmon in pellagra was organized at the Georgia State Sanitarium, in Milledgeville, in 1927. The results of this study are reported here. Canned Alaska chum salmon was used. The entire contents of the can, including bone, skin and liquid portion, were thoroughly mixed and incorporated in the cooked cereal-legume portion of the basic diet. Each patient was allowed six ounces of salmon per day, receiving approximately 1.7 ounces with the morning and evening meals, and 2.6 ounces at midday. A total calory diet of 2,050 was given daily. The basic articles of diet were cornmeal, cowpeas, wheat flour, lard and tomato juice. Cod-liver oil and calcium carbonate were also given. A total of 18 white female patients came under observation for pellagra-preventive treatment with this diet during the period of the test, all of whom remained under continuous observation for a period of not less than one year. None of these presented, at any time, any symptoms of pellagra. In the light of repeated experience it seems safe to state that, without the salmon or some other equivalent preventive, in the diet, not less than 40.50 per cent of them would have suffered a recurrence within a period of from three to seven months. The fact that none of the group showed symptoms even suggestive of pellagra would seem to be convincing evidence of the pellagra-preventive action of the salmon and of the pellagra-preventive factor in canned Alaska chum salmon. The quantity of salmon allowed was fairly liberal. Whether a smaller allowance would have been equally effective cannot be stated. The demonstration that salmon contains the pellagra-preventive factor is of considerable interest. In the first place it is a readily available preserved food, comparatively cheap, and if used in sufficient quantity, constitutes a dependable substitute for fresh meat, at least in so far as the pellagra-preventive factor is concerned. The results are also in harmony with certain previously recorded experiments showing that substances possessing black-tongue preventive potency are also preventives of pellagra, and thus furnish additional evidence that black tongue in dogs is the analogue of pellagra in man. By reason of its potency in the P-P factor, and its availability, salmon may be considered a fair substitute for meat in the areas of pellagra endemicity when meat is not readily available.

Vitamin D in Tuberculosis. By B. KRAMER, H. G. GRAYZEL, and M. J. SHEAR (Proc. Soc. f. Exper. Biol. and Med., November, 1929, p. 144).

During studies made by these workers in 1926 the question rose repeatedly as to whether vitamins play an important rôle in the etiology and treatment of tuberculosis. Ultra-violet light has in recent years been found of value in the treatment of intestinal tuberculosis; heliotherapy has been used with success in other forms of tuberculosis; calcification is often found in healed tuberculous lesions. These considerations suggested a possible linkage between tuberculosis and the vitamin D content of the diet. In the older literature, cod liver oil is mentioned as of value in the treatment of tuberculosis. This beneficial result, sometimes obtained, may not have been due to the fat

but to the vitamins present in the oil. In the present study irradiated cholesterol, cod liver oil concentrate and irradiated dried yeast powder were employed. Subsequently, biologically assayed cod liver oil was added to the number of preparations studied. Eighteen tuberculous children were divided into 2 groups of 9 each; one was the test group, the other the control. One child had tuberculosis of the skin; the others had active bone tuberculosis. All received a well-balanced diet. The treated children received daily 4 mg. irradiated ergosterol (Fleischman) during the first 4 months and 7 mg. for the succeeding 8 months (0.0001 mg. of the irradiated ergosterol per rat per day produced a continuous line in rachetic rats in 7 days). Physical examinations of the children were made periodically, as well as blood pressure readings, urine analyses, roentgenograms and analyses for serum calcium and phosphorus. The results were summarized, as follows: The daily addition of a large amount of vitamin D did not produce any detectable acceleration of the healing process. Such doses of irradiated ergosterol produced no discernible deleterious effects. The administration of irradiated ergosterol for 12 months produced no increase in either serum calcium or phosphorus.

The Effect of Restricted Diet and Suprarenalectomy on Experimental Tuberculosis in the White Rat. By MAXIM STEINBACH (Proc. Soc. f. Exper. Biol. and Med., November, 1929, page 142.)

It has been previously demonstrated that the albino rat enjoys complete immunity to infection by human tubercle bacilli in spite of the fact that the bacteria remain alive for indefinite periods and apparently multiply in the host. In the first series of experiment described 36 rats wre used and divided into 3 groups. 12 were inoculated with human, 12 with bovine and 12 with avian strains of the tubercle bacillus. All strains used were pathogenic. 6 of each of these groups were on a bread and water diet, and 6 on a full maintenance diet. Those on the restricted diet given the human and bovine strains showed no macroscopic or microscopic evidence of tissue reaction. In smears and tissue stains many of these animals showed the presence of the tubercle bacillus. 82 per cent of those inoculated with the avian strain showed extensive macroscopic lesions. The control groups were negative as to human and bovine infection, but with the avian strain 50 per cent were found at autopsy to have extensive tuberculous lesions. From these experiments it was concluded that the white rat is immune to the human and bovine strains of the tubercle bacillus, even when its resistance is lowered by a deficient diet, but is susceptible to the avian strain. It was noted, however, that a greater percentage of infections took place among those fed on a restricted diet than among those normally fed. On the basis of these conclusions it was decided to investigate the possibility of infection with the bovine as well as the avian strain in animals whose resistance is lowered by bilateral suprarenalectomy. A large number of animals were suprarenalectomized, and were subsequently inoculated on the fifth day postoperative with either bovine or avian tubercle bacilli. Most of the animals died soon after. Of those that lived, 16 had been inoculated with the bovine organism and 5 with the avian. Of the 16 animals in the bovine group, 12 survived for periods ranging from 7-22 days. Of these 12, all but one showed definite macroscopic or microscopic (or both) evidence of tubercle formation and tubercle bacilli were demonstrated in the tissues. The remaining 4 in this group were killed; three of them showed definite macroscopic lesions. In the fourth, no lesions could be found. Therefore, of the 16 animals, all but 2 showed definite evidence of tubercle formation as the result of infection with the bovine strain of tubercle bacilli. Of the 5 suprarenalectomized animals inoculated with the avian bacilli, all were found at autopsy to have extensive tuberculous lesions. In the previous experiment it was shown that only 50 per cent of normal rats inoculated with the avian strains developed characteristic tuberculous lesions. In the previous experiment it was shown that only 50 per cent of normal rats inoculated with the avian

strain developed characteristic tuberculous lesions. It was, therefore, deemed unnecessary to use additional controls for this group. It appears then that bilateral suprorenalectomy in the albino rat lowers the resistance so that subsequent inoculation with the bovine tubercle bacillus results in definite tissue reaction, with tubercle formation and caseation, resembling human tuberculosis. This does not occur in normal rats or in rats on a restricted diet. Suprarenalectomy, and to a less extent, deficient diet, increase the susceptibility of albino rats to the avian tubercle bacillus.

Reviews

Pathogenic Microörganisms. A Practical Manual for Students, Physicians and Health Officers. By WILLIAM HALLOCK PARK, M.D., Professor of Bacteriology and Hygiene, University and Bellevue Hospital Medical College and Director of the Bureau of Laboratories of the Department of Health, New York City; and ANNA WESSELS WILLIAMS, M.D., Assistant Director of the Bureau of Laboratories of the Department of Health; and CHARLES KRUMWIEDE, M.D., Assistant Director of the Bureau of Laboratories; Associate Professor of Bacteriology and Hygiene in the University and Bellevue Hospital Medical College, New York City. Ninth Edition, Enlarged and Thoroughly Revised. 819 pages, 216 engravings and 9 full-page plates. Lea and Febiger, Philadelphia, 1929. Price in cloth, $6.50 net.

The first edition of this book was called Bacteriology in Medicine and Surgery, and was written to make available for others the practical knowledge acquired in the bacteriological laboratories of the city of New York, and was intended more for medical practitioners than for medical students or laboratory workers. In the third edition the study of the pathogenic protozoa was included, and the title broadened to include the whole field of pathogenic microörganisms. At the same time the subjects were treated in a more comprehensive manner, so as to make it a suitable textbook for medical students. In the fifth edition the material was rearranged in order to bring together more closely all of the pathogenic microörganisms. In the eighth edition further rearrangements were made so that the grouping of different microörganisms conformed more closely to the classification adopted by the Society of American Bacteriologists. The new terminology was added to the older common names and several new comprehensive tabulations were given. In the present edition the many additions to our knowledge during the past three years have necessitated a very extensive revision, and many parts of the book have been completely rewritten. The sections on immunity have been amplified, particularly with reference to the experience of the authors with active immunization against diphtheria and scarlet fever. The chapters on the pyogenic cocci, paratyphoid bacilli and pneumococci have been practically rewritten. The recent additions to our knowledge of scarlet fever, measles, yellow fever, undulant fever and tularemia have been accorded due attention. Numerous other changes and additions bring this work quite up to date, and the result is a very complete and reliable textbook, well illustrated, and one thoroughly to be recommended. That it has reached its ninth edition is sufficient proof of its excellence.

Selected Readings in Pathology. From Hippocrates to Virchow. Edited by ESMOND R. LONG, Professor of Pathology, University of Chicago. 301 pages, 25 plate illustrations. Charles C. Thomas, Springfield, Illinois—Baltimore, Maryland. Price in cloth, $4.00.

This volume consists of a series of excerpts from the classics of pathology, republished in the wish to lay before physicians and medical students some of the original documents in the evolution of this fundamental branch of medical science. The works from which they are taken are constantly quoted in the class-room in pathology, but being more or less inaccessible are not often read by the student. The book does not pretend to present a connected view of the evolution of pathology, but simply to furnish, in a frankly, discontinuous way, a more intimate acquaintance with some of the greater masters of the science. Some

of the extracts are of especial historical significance as marking mile-stones in our progress in the knowledge of disease; others are representative samples of certain lengthy volumes which were of unusual influence. There are thirty-six masters represented, from Hippocrates to Virchow, including a number of less familiar names. The book serves a very useful purpose, and is to be recommended to medical students, for additional reading in courses of medical history.

Hookworm Disease. Its Distribution, Biology, Epidemiology, Pathology, Treatment and Control. By ASA C. CHANDLER, M.Sc., Ph.D., Professor of Biology, Rice Institute, Houston, Texas; Recently Officer-in-Charge, Hookworm Research Laboratory, School of Tropical Medicine and Hygiene, Calcutta, India. 494 pages, 33 figures. The MacMillan Company, New York, 1929. Price in cloth, $5.00.

Hookworm infestations are engaging the attention of the medical profession and of governments in every tropical and subtropical country in the world to a greater extent than ever before. There is probably no important and widespread human disease in which so many important and diversified contributions to knowledge have been made within the last decade, as has been the case with hookworm disease. All phases of the subject—geographic distribution, biology, epidemiology, pathology, diagnosis, treatment or control—have received attention from numerous skilled workers during this time with important results. Much of the recent work on hookworm has been made possible by the development of new research methods. Because of the great economic importance of the subject, of the great recrudescence of interest in it, and the lack of any adequate comprehensive modern account of it, the writer has attempted to bring together the work of recent years and to coordinate it with older work, in order to make it available in a convenient form for research workers, medical men and sanitarians in the many parts of the world where no such comprehensive knowledge is available in any form. This book contains a wealth of facts of greatest importance to mankind, in its relationship to problems of public health and practical medicine. It is an indispensable work to those interested in this subject. The book is well printed, and the illustrations are satisfactory.

Modern Methods of Treatment. By LOGAN CLENDENING, M.D., Professor of Clinical Medicine, Lecturer on Therapeutics, Medical Department of the University of Kansas. With Chapters on Special Subjects by H. C. ANDERSON, M.D., J. B. COWHERD, M.D., and others. Third Edition. 815 pages, 95 illustrations. C. V. Mosby and Company, St. Louis, 1929. Price in cloth, $10.00.

This third edition follows close upon the heels of the second. It has been carefully revised. The account of diathermy has been rewritten. The articles on quinidine sulphate, liver in anemia and iodine in goiter have been revised. The account of nonspecific protein therapy has been amplified, particularly as to its application to peripheral vascular disease. Synthaline, myrtillin, euphyllin, sulphocyanate, barium chloride and erysipelas antitoxin have received brief mention. The author has not endeavored to add every suggested change in therapy that has developed since the last edition, but his inclusions have been conditioned by his experience and judgment as to what methods are firmly established and supported by scientific evidence. The general plan and purpose of the book remain unchanged. This edition shows great improvement over the preceding in many sections. Others remain too superficially treated. Some discussions are excellent and notable for their common sense view.

Hemorrhoids. The Injection Treatment and Pruritus Ani. By LAURENCE GOLDBACHER, M.D. 205 pages, 31 half-tones and line engravings, some in colors. F. A. Davis Company, Philadelphia, 1930. Price in cloth, $3.50.

The purpose of this book is to present to the medical profession practical and readable information concerning hemorrhoids and pruritus ani, in as simple and brief form as

possible. A portion of the material has already been published in various medical journals, and with slight changes is here presented with the hope that it will stimulate further investigation. Hemorrhoids constitute the most frequent form of rectal disease, and are present in more than 50 per cent of patients afflicted with rectal ailments. During the World War there were 29,176 hospital admissions for hemorrhoids in the U. S. Army from April 1, 1917, to December 31, 1919, representing a total loss of 623,493 days. The actual prevalence of hemorrhoids in civil life cannot be estimated. They occur in all countries and climates and among all races, in all stations of life and in those of both sedentary and active occupation. All cases of hemorrhoids are curable, and the majority without recourse to surgery. Because of the great amount of suffering and disability produced by them, their treatment demands the prompt and serious attention of the medical profession. The author employs the incision method for the treatment of external hemorrhoids, and the injection of phenolized oil for the treatment of internal hemorrhoids and pruritus ani. In his book the general considerations of these methods, with a description of the technique employed, are given in a clear and concise manner. It is well illustrated. It is recommended to those who are interested in this subject.

College News Notes

Dr. F. M. Pottenger (Fellow), Monrovia, Calif., addressed the St. Louis Medical Society, October 29, on "The Relation of Symptoms of Disease to the Vegetative Nervous System". He also addressed the Columbus Academy of Medicine, November 4, on "Institutional Care of Tuberculosis."

Dr. C. Lydon Harrell (Associate), Norfolk, Virginia, addressed the Tidewater Dental Association, October 17, on "Co-operation of the Physicians and Dentists". On October 23, he delivered a paper before the Virginia State Medical Society at Charlottesville, entitled "Thyroid Deficiency —A Clinical Study".

Dr. Bernard L. Wyatt (Fellow), Tucson, Ariz., during October completed the incorporation of "The Wyatt Clinic".

Dr. George Morris Piersol (Fellow and Secretary-General), Philadelphia, Pa., spoke on "The Medical Society as a Teaching Institution", on November 1 at the first of a series of Postgraduate Seminars under the auspices of the Philadelphia County Medical Society.

Dr. G. Harlan Wells (Fellow), Physician-in-chief, Hahnemann Hospital, Philadelphia, recently described in detail "The Differential Diagnosis of Anemia", in a Medical Clinic at the Hahnemann Medical College.

The following Fellows of the College are among the speakers for the Postgraduate Seminars under the auspices of the Philadelphia County Medical Society:

Dr. Martin E. Rehfuss (Fellow), "How frequently is Dyspnea a matter of Simple Dietary Perversion?".

Dr. S. Calvin Smith (Fellow), "Sudden Heart Failure".

Dr. H. R. M. Landis (Fellow), "Non-Tuberculosis Lung Lesions of Upper Lobe."

Dr. E. J. C. Beardsley (Fellow and Governor), "Clinical Demonstration of Chest Examinations".

Dr. Franklin H. Martin, Director-General of the American College of Surgeons, advises that "In behalf of the officers and Regents of the American College of Surgeons, may I take this early opportunity to advise you that the next annual Clinical Congress of the College is to be held in Philadelphia, Pa., October 13-17, 1930".

The 59th Annual Meeting of the American Public Health Association will be held in Fort Worth, Texas, during the week of October 27, 1930, with the Hotel Texas as headquarters. Mr. Homer N. Calver, 370 Seventh Avenue, New York City, is the Executive Secretary.

The following members of the College are scheduled to speak at the "Health Talks" for the public under the auspices of the Philadelphia County Medical Society:

Dr. James M. Anders (Master), "Where is the Layman Remiss in the Care of his Health?"

Dr. William Devitt (Fellow), of Devitt's Camp, Allenwood, Pa., "Diet and Dissipation and Tuberculosis".

Dr. George E. Pfahler (Fellow), Cancer—the Prevention of its Increase".

Dr. Carl V. Vischer (Fellow), Philadelphia, is co-author with Dr. Edwin O. Geckler and Dr. Grant O. Favorite of a "Report of Arthritis Conference, Hahnemann Hospital". This report was read at the meeting of the Homeopathic Medical Society of the State of Pennsylvania and was published in the November number of the Hahnemannian Monthly.

The following Fellows of the College were elected Officers of the Homeopathic Medical Society of the State of Pennsylvania:

1st Vice President—Dr. Henry I. Klopp, Allentown, Pa.

Secretary—Dr. E. Roland Snader, Philadelphia, Pa.

Dr. Lewellys F. Barker (Fellow), Baltimore, Md., succeeds Dr. Ray Lyman Wilbur as Chairman of the Medical Council of the U. S. Veterans' Bureau.

Dr. Emanuel Libman (Fellow), New York, addressed the Pittsburgh Medical Forum, October 26, on "Observations on Angina Pectoris of Various Origins."

Dr. David C. Hall (Fellow), Seattle, upon invitation of the Pan-Pacific Surgical Conference, issued by the Pan-Pacific Union, read a paper upon the medical aspects of Goiter in relation to surgery. The Conference was held in Honolulu, T. H., during August. Nearly two hundred surgeons from all countries bordering the Pacific were in attendance.

Dr. George B. Lake (Associate), Chicago, spoke, under the auspices of the Illinois State Medical Society, before the Parent-Teacher Association of Waukegan, Ill., on November 19, and before the University Club at Peoria, Ill., on November 26, his subject being, "Psychic Diseases and a Philosophy of Life".

The following Fellows of the College are members of the National Board of Medical Examiners of the United States:

Walter L. Bierring, Des Moines, Iowa.
Lewis A. Conner, New York, N. Y.
Hugh S. Cumming, Washington, D. C.
R. D. Harden, Washington, D. C.
M. W. Ireland, Washington, D. C.
Howard T. Karsner, Cleveland, Ohio.
W. S. Leathers, Nashville, Tenn.
George W. McCoy, Washington, D. C.
C. E. Riggs, Washington, D. C.

Dr. Walter L. Bierring is now President.

Dr. Harold Swanberg (Fellow), Quincy, Ill., addressed the annual meeting of the Northeast Missouri Dental Society at Hannibal, October 21, on "The Role of the Maxillary Sinus in General Infections".

Dr. William M. James (Fellow) of the Herrick Clinic, Panama, R. P., has been invited by the University of London to deliver a course of six lectures on Tropical Medicine during 1930.

Dr. Lyell C. Kinney (Fellow), San Diego, Calif., at the annual meeting held recently in Coronado, was elected President-Elect of the California Medical Association.

Dr. Benjamin Hobson Frayser (Fellow), Fort Harrison, Mont., was recently elected Surgeon-General of the national organization of the American War Veterans. Dr. Frayser has also been appointed District Deputy for the States of Wyoming, Idaho, and Montana, Theta Nu Epsilon Society.

Dr. Henry W. Grote, Bloomington, Illinois, has been re-instated as an active Associate of the College.

Dr. Henry J. John (Fellow), Cleveland, addressed the Tulsa (Okla.) Academy of Medicine, November 18, on "Diabetes".

A portrait of the late Dr. Arthur S. Loevenhart (Fellow), has been hung in the Auditorium of the Memorial Institute of the Wisconsin General Hospital at Madison. Dr. Loevenhart was formerly head of the Department of Pharmacology of the University of Wisconsin Medical School.

Dr. P. P. McCain (Fellow), Sanatorium, N. C., has been elected President of the Southern Tuberculosis Conference.

Dr. L. R. DeBuys (Fellow), New Orleans, recently resigned as Professor of Pediatrics and head of that department of Tulane University School of Medicine, a post he has held for eight years. He is

succeeded by Dr. Robert A. Strong of Pass Christian, Mississippi.

Dr. Lawrason Brown (Fellow), Saranac Lake, will be one of the speakers at the Pan-American Medical Association meeting at Panama City, January 30-February 3.

Dr. William Gerry Morgan (Fellow), President-Elect of the American Medical Association was the recipient of an honorary meeting and dinner held in Washington, December 11, by the Medical Society of the District of Columbia. Civic as well as medical leaders of the community were in attendance, and a program suitable for the occasion was rendered. Dr. Frank Leech (Fellow), Washington, was the Chairman of the Committee on Arrangements.

Dr. Howard M. Jamieson (Fellow), Decatur, Ill., addressed the Illinois Medical Library Association, December 5, on "Some notes on Diagnosis of Carcinoma of the Blood Serum".

Dr. Cyrus C. Sturgis (Fellow), Professor of Internal Medicine at the University of Michigan Medical School, spoke before the Wayne County Medical Society at Detroit, November 19, his subject being "Treatment of Pernicious Anemia with Special Reference to Some Newer Methods".

Dr. George C. Hale (Fellow), Professor and Chief of the Department of Medicine of the University of Western Ontario, London, Canada, gave a diagnostic clinic before the Highland Park Physicians' Club, December 5.

Dr. John D. Wilson (Fellow), Scranton, Pa., is a member of the Board of Directors of the Pennsylvania unit of the National Association Against the Prohibition Amendment.

Dr. Francis D. Murphy (Fellow), Wauwatosa, Wis., recently addressed the Kenosha County Medical Society on Chronic Glomerulonephritis.

Dr. Andrew C. Ivy (Fellow), Chicago, addressed the Milwaukee Academy of Medicine, October 22, on "The Mechanics of Digestion with Special Reference to Bile Flow".

Dr. David P. Scott (Fellow), Lynchburg, Va., delivered an address on "Medical Treatment" before the South Piedmont, (Va.) Medical Society on November 26.

Dr. William A. White (Fellow), Superintendent of St. Elizabeth's Hospital, Washington, D. C., reviewed the past twenty years of work of the mental hygiene movement and discussed the coming International Congress on Mental Hygiene to be held in Washington next May, at the dinner celebrating the twentieth anniversary of the movement held in New York, November 1.

Dr. B. M. Riley (Fellow), Omaha, Nebr., is the author of a paper entitled "Two Types of Vascular Disturbances of the Extremities", appearing in the December issue of the Nebraska State Medical Journal.

Dr. Solomon Strouse (Fellow), Chicago, addressed the Cincinnati College of Medicine, November 14, on "Obesity".

Dr. Hugh A. McGuigan (Fellow)' Chicago, addressed the Medico-Historical Club of the University of Illinois College of Medicine, November 7, on "A Sabbatical Year in Europe", illustrated with lantern slides.

Dr. Carl J. Wiggers (Fellow), Cleveland, addressed the Chicago Medical Society, November 20, his title being "The Clinical Physiology of Aortic Insufficiency".

Dr. George G. Ornstein (Fellow), is now Associate Clinical Professor of Medicine at the New York Postgraduate Medical School and Hospital.

OBITUARY

Dr. Peter J. Calvy (Fellow), Fond du Lac, Wisconsin, died during October, 1929, aged 55.

Dr. Calvy received his medical training at the Wisconsin College of Physicians and Surgeons, graduating in 1903. He had been a teacher of nervous and mental diseases of medical practice at the St. Agnes Training School for Nurses for some years. He was a member of the Fond du Lac County Medical Society, the Wisconsin State Medical Association, a Fellow of the American Medical Association and a Fellow of the American College of Physicians since April, 1920.

Dr. Stillman Smith Ham (Fellow), Schenectady, N. Y., died at his home, 1503 Union Street, December 9, 1929, of an acute heart attack. He had been in apparent good health, and had been receiving patients up to a half hour before his sudden death.

Dr. Ham was born in Schenectady, February 23, 1878. He received his PhB. degree from Union College in 1899, and his medical degree from the Albany Medical College in 1902.

From 1904 to 1914, Dr. Ham was physician to the Day Nursery Dispensary and to the Children's Home, both of Schenectady. From 1917 to 1927, he was physician to the Old Ladies Home. Since 1919 he had been attending physician to the Ellis Hospital, and clinical instructor at the same institution for medical students of the Albany Medical College since 1920. For many years he was chief medical examiner for the Metropolitan Life Insurance Company.

Dr. Ham was a captain in the medical corps of the Army during the World War, serving at Camp Gordon, Atlanta, Ga.

He was a member of the Schenectady County Medical Society (President, 1919), the New York State Medical Society and the American Medical Association. He became a Fellow of the American College of Physicians on April 10, 1917, having been one of the very early members. Dr. Ham was highly esteemed and respected by all who knew him.

REPORT, COMMITTEE ON NOMINATIONS

The Committee on Nominations, appointed by the President in accordance with the provisions of the By-Laws, respectfully presents the followiong nominees for the line offices of the American College of Physicians for 1930-31:

President .....Sydney R. Miller, Baltimore, Md.
President-Elect: .....S. Marx White, Minneapolis, Minn.
1st Vice President: .....Aldred Scott Warthin, Ann Arbor, Mich.
2nd Vice President: .....Francis M. Pottenger, Monrovia, Calif.
3rd Vice President: .....John A. Lichty, Clifton Springs, N. Y.

W. Blair Stewart, Chairman
E. B. Bradley
James S. McLester
James H. Means
Charles F. Martin

LIFE MEMBERSHIP

Three years ago the Board of Regents, believing a sound financial foundation to be one of the best guarantees of insuring the stability and perpetuity of the American College of Physicians, provided for the building up of an Endowment Fund, "the principal of which shall be held intact and invested in securities approved by the Board of Regents, while the income shall be available for carrying out the purposes of the organization" (See By-Laws, Article VIII).

This Endowment Fund "shall consist of: (1) all moneys received for LIFE MEMBERSHIP in the College; (2) such moneys as may be set aside by the Board of Regents from time to time from the funds of the College, and (3) such moneys as may be donated directly to the fund."

The then President and President-Elect, Dr. Alfred Stengel and Dr. Frank Smithies, respectively, set the precedent by immediately subscribing $500.00 each to the Fund by becoming Life Members. Since that time, several more Fellows have subscribed to Life Membership, some by full payment and others by subscribing $100.00 per year for four years, which together with the $100.00 initial Fellowship fee paid at time of election will amount to $500.00. Total payments already made amount to $4,700.00. This fund is already invested in securities approved by the Board of Regents.

The following constitutes the present list of Life Members:

Lewellys F. Barker, Baltimore, Md.
Oscar Berghausen, Cincinnati, Ohio.
Robert Bernhard, New Orleans, La.
Carl R. Comstock, Saratoga Springs, N. Y.
Charles F. Martin, Montreal, Que.
Nels C. Meling, Evanston, Ill.
John G. Ryan, Denver, Colo.
Adolph Sachs, Omaha, Nebr.
Frank Smithies, Chicago, Ill.
Alfred Stengel, Philadelphia, Pa.
Noxon Toomey, St. Louis, Mo.
M. Lawrence Turner, Berwyn, Md.
A. H. Waterman, Chicago, Ill.
Bernard L. Wyatt, Tucson, Ariz.

Life Members pay no more dues for the balance of their lives; they receive the official journal, Annals of Internal Medicine, without further cost; they receive the Directory every time revised and re-published, as well as other publications the College may have from time to time; they receive an engraved Life Membership Card, admitting them to every meeting and entitling them to take part in all College activities; their names will be engrossed on the permanent scroll of Contributors to the College Endowment Fund; they will be helping to build up a fund which will eventually enable the College to carry out a larger and more active program in the field of Internal Medicine.

Subscription Form

ENDOWMENT FUND

LIFE MEMBERSHIP

I hereby subscribe Five Hundred Dollars ($500) to the Endowment Fund of the American College of Physicians, the amount to include the $100 paid already by me as my Fellowship fee at time of Election. I elect the option checked below for the payment of the balance, $400.

A. Payable in one lump sum during the present year.

B. Payable in four annual installments of $100 each, beginning....., 19 .

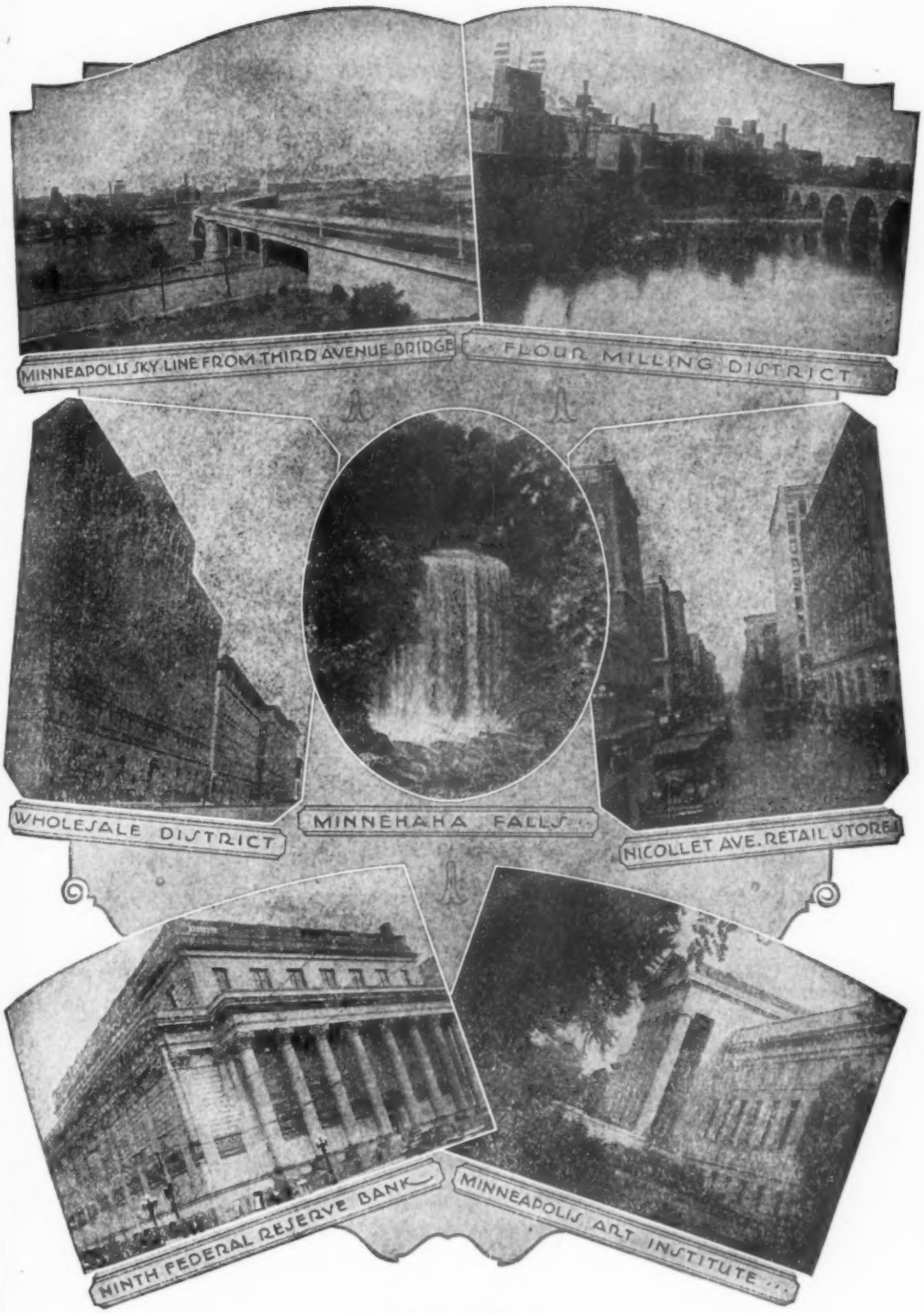
My annual dues shall cease at once if I elect Option A; or, if I elect Option B, when I have made three annual payments ($300, total).

Upon full payment of this subscription, the sum of $500 shall be credited to and become a part of the Permanent Endowment Fund of the College, and I shall become a LIFE MEMBER of the College.

Name .....

Date..... Address .....

In case of death, all unpaid balances will be cancelled.



MINNEAPOLIS SCENES

WHERE WE MEET — FEBRUARY 10-14, 1930

FOURTEENTH ANNUAL CLINICAL SESSION

AMERICAN COLLEGE OF PHYSICIANS

Fourteenth Annual Clinical Session

Minneapolis, Minnesota

February 10-14, 1930

MONDAY, FEBRUARY 10

Morning: Registration
Afternoon: Opening Session, which will include the addresses of Welcome and part of the Scientific Session.
Evening: Scientific Program

TUESDAY, FEBRUARY 11

Morning: Clinics
Afternoon: Scientific Session
Evening: Scientific Session

WEDNESDAY, FEBRUARY 12

Morning: Clinics
Afternoon: Scientific Session
Evening: Convocation, followed by Smoker

THURSDAY, FEBRUARY 13

Morning: Clinics
Afternoon: Scientific Session, short, followed by General Business Meeting at 4:00
Evening: Banquet

FRIDAY, FEBRUARY 14

Morning: Clinics
Afternoon: Scientific Session

INDEX TO PLACE OF MEETING, CLINICS AND DEMONSTRATIONS

(Registration, Information, Scientific Sessions and Convocation at the Auditorium.)

A University Hospitals.
Lecture Room, Todd Memorial Hospital.
B University Hospitals.
Lecture Room, Eustis Memorial Hospital.
C Institute of Anatomy, University of Minnesota.
D Veterinary Building, University Farm, St. Paul.
E Hennepin County Medical Society Assembly Room.
F Minneapolis General Hospital.
Sun Porch.
G Minneapolis General Hospital.
Clinic Room.
H St. Mary's Hospital.
I Swedish Hospital.
J Abbott Hospital.
K Northwestern Hospital.
L Glen Lake Sanatorium.

AUDITORIUM

The place of meeting for the Opening Session Monday afternoon, Scientific Sessions Tuesday to Friday afternoons and Monday and Tuesday evenings, and for the Convocation, followed by the Smoker, Wednesday evening.

Registration and Information Booths and the Commercial Exhibits are all comfortably housed on the same floor with the place of meeting, and ample provision is made for all the activities surrounding the Sessions.

Grant Street between Stevens Avenue and Third Avenue South.

CLINICS AND DEMONSTRATIONS

A-B University Hospitals: Elliott Memorial, Todd Memorial (Eye, Ear, Nose and Throat), Cancer Institute, Eustis Memorial (Pediatrics), Students' Health Service, together with the Out-Patient Department. 400 beds.

A Amphitheater, Todd Memorial Hospital.
Seating capacity 150.

B Amphitheater, Eustis Memorial Hospital.
Seating capacity 150.
"Minneapolis-St. Paul" streetcars, east-bound, on Fifth Street at Hennepin, Nicollet or Marquette Avenues (20 minutes) or bus, "St. Paul via University Avenue" on Seventh Street at Hennepin, Nicollet or Marquette Avenues, or at Radisson Hotel (15 minutes).

C Institute of Anatomy, University of Minnesota Medical School. Laboratories of Pathology, Anatomy and allied branches. Auditorium seating capacity 226. Washington Avenue at Church Street, S.E. "Minneapolis-St. Paul streetcars, east-bound, on Fifth Street at Hennepin, Nicollet or Marquette Avenues (20 minutes) or bus, "St. Paul via University Avenue" on Seventh Street at Hennepin, Nicollet or Marquette Avenues, or at Radisson Hotel (15 minutes).

D Veterinary Building, University Farm.
Agricultural, Veterinary and Home Economics.
Departments of University of Minnesota.
St. Anthony Park. Seating capacity 125.
Como Avenue streetcar, east-bound, on Hennepin Avenue to Doswell Avenue. Special bus for members of The College leaves Nicollet Hotel 7:45 A.M., and takes on passengers at the Radisson, Dyckman, Curtis and Leamington Hotels.

E Hennepin County Medical Society Assembly Room and Library. Twentieth Floor of Medical Arts Building on Ninth Street South, between Nicollet and Marquette Avenues.
Seating capacity 350.
In Loop. Walking distance from hotels.

F-G Minneapolis General Hospital (Municipal). 689 Beds. Entrance on Fifth Street South, between Sixth and Seventh Avenues.

F Sun Porch, second floor. Seating capacity 125.

G Clinic Room, basement floor.
Seating capacity 70.
Chicago Avenue streetcar, south-bound, crosses Hennepin, Nicollet and Marquette Avenues at Eighth Street (10 minutes).

H St. Mary's Hospital. 2500 Sixth Street South.
General. 350 beds (100 children).
Seating capacity 400.
Seventh Street-Minnehaha-Hazel Park streetcar, south-bound, on Washington Avenue at Hennepin, Nicollet or Marquette Avenues. Get off at 25th and Riverside. 20 minutes from Loop.

I Swedish Hospital. New Building, Eighth Street at Ninth Avenue South. General. 320 beds.
Seating capacity 100.
Bloomington-Columbia Heights streetcar, east-bound, at Second Avenue and Fourth Street South. Get off at Tenth Avenue South (10 minutes from Loop).

J Abbott Hospital. 1717 First Avenue South. 106 beds. (50 pediatrics). Seating capacity 60.
Nicollet Avenue streetcar, south-bound, on Marquette Avenue, to Eighteenth Street. 5 minutes from Loop. Walking distance from Auditorium.

K Northwestern Hospital. 2627 Chicago Avenue. General. 200 beds. Seating capacity 100.
Chicago Avenue streetcar, southbound, on Eighth Street South at Hennepin, Nicollet or Marquette Avenues, to 27th Street South. 20 minutes from Loop.

L Glen Lake Sanatorium. Hennepin County Tuberculosis Sanatorium. 700 beds (60 children).
Seating capacity 400.
Bus at Union Bus Station, Seventh Street and First Avenue North. Special bus for members of The College leaves the Nicollet Hotel at 7:45 A.M. and takes on passengers at Radisson, Dyckman, Curtis and Leamington Hotels.

Note:

Hennepin, Nicollet and Marquette Avenues, the principal thoroughfares, lie approximately parallel, and are crossed by the numbered streets. Washington Avenue, upon which are located the Post-Office and the Milwaukee Station, lies between Second and Third Streets. Grant Street, upon which the Municipal Auditorium faces, corresponds to Thirteenth Street.

The taxicab fare in the Loop district is twenty-five cents from railway stations to hotels or to the Municipal Auditorium.

The taxicab care to any hospital in this city does not exceed seventy cents, with no charge for extra passengers.

Bus service is provided to the Veterinary Building, University Farm and to Glen Lake Sanatorium and these leave on schedule. The bus fare to the former is fifty cents round trip and to the latter seventy-five cents round trip. In case taxicabs are necessary or desired, note that the rate per cab to the University Farm is $1.30 and to Glen Lake Sanatorium $4.00, these being independent of the number of passengers.

PROGRAM FOURTEENTH ANNUAL CLINICAL SESSION

MINNEAPOLIS COMMITTEES

S. Marx White, General Chairman

EXECUTIVE COMMITTEE

S. Marx White—Chairman
Henry L. Ulrich
E. L. Gardner
Olga S. Hansen—Secretary

COMMITTEE ON CONVOCATION AND ENTERTAINMENT

J. Fowler Avery—Chairman
F. L. Jennings
Archie Beard
Samuel A. Weisman

COMMITTEE ON AUDITORIUM AND TRANSPORTATION

Charles R. Drake—Chairman
Clifford E. Henry
Hugo O. Altnow

COMMITTEE ON CLINICS AND DEMONSTRATIONS

Henry L. Ulrich—Chairman

Moses Barron
Hilding Berglund
Charles R. Drake
George E. Fahr
E. L. Gardner
F. L. Jennings
E. S. Mariette
J. Arthur Myers
W. A. O'Brien
T. A. Peppard

Robert I. Rizer

COMMITTEE ON HOTELS

Norman M. Smith—Chairman
Frederick H. K. Schaaf
Arthur A. Wohlrabe

COMMITTEE ON PUBLICITY

J. Arthur Myers—Chairman
(Co-operating with the Committee on Publicity of the Hennepin County Medical Society.)

COMMITTEE ON ENTERTAINMENT OF VISITING WOMEN

Mrs. E. S. Mariette—Chairman

Mrs. H. O. Altnow
Mrs. J. Fowler Avery
Mrs. Moses Barron
Mrs. Charles R. Drake
Mrs. George E. Fahr
Mrs. Everett Geer
Mrs. Clifford E. Henry
Mrs. F. L. Jennings
Mrs. J. Arthur Myers
Mrs. Robert I. Rizer
Mrs. Fredk. H. K. Schaaf
Mrs. Norman M. Smith
Mrs. Clyde A. Undine
Mrs. S. A. Weisman
Mrs. Arthur Wohlrabe
Dr. Olga S. Hansen

FINAL PROGRAM

ANNUAL CLINICAL SESSION
THE AMERICAN COLLEGE OF PHYSICIANS

February 10-14, 1930

Monday, February 10, 1930

OPENING SESSION, 2:30 O'CLOCK

The Auditorium

1. Addresses of Welcome.
   Lotus Delta Coffman, President of the University of Minnesota.
   Elias P. Lyon, Dean of the University of Minnesota Medical School.
   Edward L. Tuohy, Duluth,
   President of the Minnesota Society of Internal Medicine.
   S. H. Boyer, Duluth,
   President of the Minnesota State Medical Association.
   E. L. Gardner, Minneapolis,
   President of the Hennepin County Medical Society.
2. Reply to Addresses of Welcome.
   John H. Musser, Jr., New Orleans,
   President of The American College of Physicians.
3. Colloids in Medicine.
   Ross A. Gortner, University of Minnesota.
4. Cerebral Localization.
   Lewis J. Pollock, Chicago.
5. The Psychological Panel in Diagnosis and Prognosis.
   Walter Freeman, Washington, D. C.
6. Gastro-Intestinal Troubles that Now Go Undiagnosed.
   Walter C. Alvarez, Rochester, Minn.

(Monday, February 10, 1930)

EVENING SESSION, 8:00 O'CLOCK

The Auditorium

1. Latent Hyperthyroidism Masked as Heart Disease.
   Samuel A. Levine, Boston.
2. Observations on the Etiology of Gall-Stones.
   A. C. Ivy, Chicago.
3. The Significance of Atelectasis in Bronchopulmonary Conditions.
   Frederick T. Lord, Boston.
4. Moving Pictures of the Results of Stramonium Treatment in Encephalitis.
   Frederick Epplen, and (by invitation) A. L. Jacobson, Seattle.

Tuesday, February 11, 1930

MORNING, 9:00 TO 12:00 O'CLOCK
Clinics and Demonstrations

AFTERNOON, 2:00 O'CLOCK

The Auditorium

VASCULAR DISEASE

1. The Effect of Generalized Arteriosclerosis upon the Heart and the Systematic Circulation.
   George E. Fahr, Minneapolis.
2. Some Newer Aspects in the Problem of Essential Hypertension.
   Norman M. Keith and James W. Kernohan, Rochester, Minn.
3. The Retinal Vascular Changes in Hypertension.
   Henry P. Wagner, Rochester, Minn.
4. Arteriosclerosis in Diabetes.
   Elliott P. Joslin, Boston.
5. The Relations of Arterial Sclerosis and Renal Disease.
   Alfred Stengel, Philadelphia.
6. The Causes of Arterial Hypertension.
   E. T. Bell, Minneapolis.
7. The Management of Hypertension.
   James S. McLester, Birmingham.
8. The New Possibilities in Classification and Treatment of Anemia.
   Hilding Berglund, Minneapolis.
9. Cinematomicrographic Demonstration of Human Intestinal Protozoa. Pictures and Remarks on their Biology, Pathology and Treatment.
   John V. Barrow, Los Angeles.

(Tuesday, February 11, 1930)

EVENING, 8:00 O'CLOCK

The Auditorium

1. History of Syphilis.
   Joseph L. Miller, Chicago.
2. History of Certain Medical Instruments of Precision.
   Logan Clendening, Kansas City, Mo.
3. Spontaneous Pneumothorax, Non-tuberculouss.
   F. J. Hirschboeck, Duluth, Minn.
4. The Healing of Tuberculosis, Illustrated by Films and Slides.
   Francis M. Pottenger, Monrovia, Calif.

Wednesday, February 12, 1930

MORNING, 9:00 TO 12:00 O'CLOCK
Clinics and Demonstrations

AFTERNOON, 2:00 O'CLOCK

The Auditorium

1. Splenic Puncture as a Diagnostic Procedure in Infancy and Childhood.
   Julius H. Hess, Chicago.
2. I. Diagnostic and Physiologic Studies in Certain Forms of Scleroderma.
   George E. Brown and Paul A. O'Leary, Rochester, Minn.
   II. Surgical Indications and Operative Results in the Treatment of Vasospastic Types of Scleroderma, with Sympathetic Ganglionectomy.
   A. W. Adson, Rochester, Minn.
3. Sympathectomy in Polyarthritis.
   Leonard G. Rowntree, Rochester, Minn.
4. The Relation of Experimental Rheumatoid Inflammation to Allergy.
   Benjamin J. Clawson, Minneapolis.
5. In Defense of the Stethoscope.
   James B. Herrick, Chicago.
6. Rectal Temperature Curves; Normal and Abnormal.
   William B. Breed, Boston.
7. The Limitations of Heliotherapy in Pulmonary Tuberculosis.
   Bernard L. Wyatt, Tucson.
8. Resumé of Our Present Attitude Regarding Iodine in the Treatment of Toxic Goiter.
   James H. Means, Boston.
9. Unusual Addison's Syndromes.
   A. B. Brower, Dayton, Ohio.
10. A New Method for the Treatment of Pellagra.
    Clyde Brooks, University, Alabama.
11. Multiple Polyposis of the Colon.
    J. A. Bargen, Rochester, Minn.

(Wednesday, February 12, 1930)

EVENING, 8:00 O'CLOCK

The Auditorium

CONVOCATION OF THE COLLEGE

The General Profession is cordially invited. No special admission tickets are required.

1. Convocation Ceremony.
2. President's Address.
   John H. Musser, Jr., New Orleans.

SMOKER

The Smoker will follow the Convocation Exercises, after a brief intermission. An attractive program has been arranged.

Thursday, February 13, 1930

MORNING, 9:00 TO 12:00 O'CLOCK
Clinics and Demonstrations

AFTERNOON, 2:00 O'CLOCK
The Auditorium

1. Symposium on The Biology of Cancer.
   The Etiology and Biology of Cancer.
   Leo Loeb, St. Louis.
   The Nature of Heredity in Animals.
   H. Gideon Wells, Chicago.
   Heredity of Cancer in Man.
   Aldred Scott Warthin, Ann Arbor.
   The Principles of Radiation Treatment.
   Francis Carter Wood, New York.

2. Undulant Fever in California.
   J. Edward Harbinson, Woodland, Calif.

3. Undulant Fever; A Clinicopathological Study.
   Walter M. Simpson, Dayton, Ohio.

4. Curing the Ulcer Patient.
   Seale Harris, Birmingham.

The General Business Meeting of The College will be held at 4:00 o'clock in the Auditorium. All Masters and Fellows should attend.

Thursday, February 13, 1930

EVENING, 7:00 O'CLOCK
The Curtis Hotel

THE ANNUAL BANQUET OF THE COLLEGE
(Procure tickets at the Registration Bureau.)

A Dance will follow the Banquet.

Friday, February 14, 1930

MORNING, 9:00 TO 12:00 O'CLOCK
Clinics and Demonstrations

AFTERNOON, 2:00 O'CLOCK
The Auditorium

1. Some Observations of Functional Diseases of the Alimentary Tract.
   William Gerry Morgan, Washington, D. C.

2. Remarks on Chronic Infections.
   Allen K. Krause, Tucson.

3. Symposium on The Rôle of Surgery in Pulmonary Tuberculosis.
   Pneumothorax.
   James Burns Amberson, Loomis, N. Y.

Pneumolysis.
Ralph C. Matson, Portland, Ore.
Multiple Intercostal Neurectomy and Phrenicectomy.
John Alexander, Ann Arbor.
Thoracoplasty.
Philip King Brown, San Francisco.
General Consideration of the Rôle of Surgery in Tuberculosis.
Gerald Webb, Colorado Springs.

4. The Diagnosis of Pre-Clinical or Latent Tubercle by Caulfeild's Inhibitive and the T. C. F. (with Lantern Slides of Chests and Graphs.)
W. E. Ogden, Toronto.
5. A Diagnostic Triad in Syphilitic Aortitis.
C. Saul Danzer, Brooklyn.

PROGRAM OF CLINICS

A Tuesday, February 11, 1930

UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA
(Union and Delaware Streets, S. E.)
Todd Amphitheatre
(Capacity—160)

9:00- 9:30 Testing Gastric Function.
Hilding Berglund.
9:30-10:00 X-ray Treatment of Hyperthyroidism.
W. Stenstrom and Karl Anderson.
10:00-10:30 Oesophagograms in Heart Diagnosis.
Leo Rigler.
10:30-11:30 The Clinical Development of Rheumatic Heart Disease.
S. A. Levine, Boston.
11:30-12:00 Circulatory Tests Previous to Amputation.
W. T. Peyton.

A Wednesday, February 12, 1930

UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA
(Union and Delaware Streets, S. E.)
Todd Amphitheatre
(Capacity—160)

9:00- 9:30 Purpura.
Henry L. Ulrich.
9:30-10:00 Rare Forms of Myelosis.
Hal Downey.
10:00-10:30 Secondary Anemias.
Hilding Berglund.
10:30-11:00 Lymphatic Leukemia and Aplastic Anemia.
M. Fallon and W. A. O'Brien.
11:00-11:30 Syphilitic Heart Disease.
J. H. Musser, New Orleans.
11:30-12:00 Skin Clinic.
H. E. Michelson.

A Thursday, February 13, 1930

UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA
(Union and Delaware Streets, S. E.)
Todd Amphitheatre
(Capacity—160)

9:00- 9:30 Coarctation of Aorta.
Henry L. Ulrich.
9:30-10:30 Scleros of Pulmonary Artery.
Henry L. Ulrich and W. A. O'Brien.
10:00-11:00 The Heart in Pregnancy.
S. Marx White and Jennings C. Litzenberg.
11:00-11:30 Fulminating Hypertension.
Richard Johnson and W. A. O'Brien.
11:30-12:00 Congenital Heart.
M. J. Shapiro.

A Friday, February 14, 1930

UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA
(Union and Delaware Streets, S. E.)
Todd Amphitheatre
(Capacity—160)

9:00- 9:30 Endothelioma.
W. A. O'Brien and L. G. Rigler.
9:30-10:00 Tumors of the Oesophagus.
W. A. O'Brien and K. Phelps.
10:00-10:30 Cancer of the Stomach.
Karl Anderson and L. G. Rigler.
10:30-11:00 Cancer of the Head and Neck.
Carl Waldron.
11:00-11:30 Cancer of the Rectum.
A. C. Strachauer.
11:30-12:00 Myeloma.
H. Berglund and L. G. Rigler.

A Tuesday, February 11, 1930

UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA
(Union and Delaware Streets, S. E.)
Eustis Amphitheatre
(Capacity—150)

9:00- 9:30 Ulcerative Colitis.
Karl Anderson.
9:30-10:00 X-ray Diagnosis of Small Pleuritic Exudates.
Leo Rigler.
10:00-10:30 Bronchiectasis.
Kenneth Phelps.
10:30-11:30 Chronic Arthritis.
J. L. Miller, Chicago.
11:30-12:00 Pancreatic Cyst.
Owen Wangensteen.

B Wednesday, February 12, 1930

UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA
(Union and Delaware Streets, S. E.)
Eustis Amphitheatre
(Capacity—150)

9:00-10:00 Bowel Obstruction.
Owen Wangensteen.
10:00-11:00 Medical Clinic.
E. L. Tuohy, Duluth.
11:00-11:30 Embolectomy.
W. T. Peyton.
11:30-12:00 Treatment of Varicose Veins.
J. M. Hayes.

B Thursday, February 13, 1930

UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA
(Union and Delaware Streets, S. E.)
Eustis Amphitheatre
(Capacity—150)

9:00- 9:30 Pediatric Clinic.
F. W. Schultz.
9:30-10:00 Hydrocephalus Treated with Diuretin.
C. A. Stewart.
10:00-11:00 Pediatric Clinic.
Julius Hess, Chicago.
11:00-11:30 Orthopedic Clinic.
W. H. Cole, St. Paul.
11:30-12:00 Tuberculosis in Childhood.
J. A. Myers.

B Friday, February 14, 1930

UNIVERSITY HOSPITALS, UNIVERSITY OF MINNESOTA
(Union and Delaware Streets, S. E.)
Eustis Amphitheatre
(Capacity—150)

9:00- 9:30 Nephrosis.
Hilding Berglund.
9:30-10:00 Hodgkin's Disease.
Reuben Johnson and W. Stenstrom.
10:00-10:30 The Eye in Cardio-Renal Disease.
F. E. Burch.
10:00-11:30 Vibration Sense and New Method for Its Quantitative Testing.
J. C. McKinley and R. Gray.
11:30-12:00 Gynecological Problems for the Internist.
Jennings C. Litzenberg.

C

Tuesday, February 11, 1930

INSTITUTE OF ANATOMY, UNIVERSITY OF MINNESOTA
(Washington Avenue near Church Street, S. E.)
Room 102, First Floor
(Capacity—226)

9:00- 9:30 Study of Malnutrition.
C. M. Jackson.
9:30-10:00 Growth and Development.
R. E. Scammon.
10:00-10:30 Innervation of Chest.
A. T. Rasmussen.
10:30-11:30 Rôle of Vitamines.
G. O. Burr.
11:00-11:30 Deficiency Diet and Sterility.
J. A. Urner.
11:30-12:00 Problems in Hematology.
Hal. Downey.

C

Wednesday, February 12, 1930

INSTITUTE OF ANATOMY, UNIVERSITY OF MINNESOTA
(Washington Avenue near Church Street, S. E.)
Room 102, First Floor
(Capacity—226)

9:00- 9:30 Carcinoid Tumors of Ileum.
Hamilton Cooke.
9:30-10:00 Studies in Rheumatic Fever.
B. J. Clawson.
10:00-10:30 Differential Diagnosis of Hodgkin's Disease, Leukemia, Lymphosarcoma.
J. S. McCartney.
10:30-11:00 Recent Advances in Pharmacology.
A. D. Hirschfelder.
11:00-12:00 Demonstration of Secretion of Urine in Kidney.
R. N. Bieter.

C

Thursday, February 13, 1930

INSTITUTE OF ANATOMY, UNIVERSITY OF MINNESOTA
(Washington Avenue near Church Street, S. E.)
Room 102, First Floor
(Capacity—226)

9:00- 9:30 Distribution of Iodin and Goiter.
J. F. McClendon.
9:30-10:00 Bile Salt Determinations.
T. A. Pascoe and R. L. Gregory.
10:00-10:30 The Allergy Problem for Internists.
W. P. Larson.
10:30-11:00 Parasitology and Disease.
W. A. Riley.
11:00-11:30 The Higher Fungi.
A. T. Henrici.
11:30-12:00 Tularemia in Man and Annimals.
R. G. Green.

C Friday, February 14, 1930

INSTITUTE OF ANATOMY, UNIVERSITY OF MINNESOTA
(Washington Avenue near Church Street, S. E.)
Room 102, First Floor
(Capacity—226)

9:00- 9:30 Student Health Service.
H. S. Diehl.

9:30-10:00 Studies in Tuberculosis in University Students.
J. A. Myers.

10:00-10:30 Periodic Health Examination in University Students.
H. D. Lees.

10:30-11:00 Hypertension Studies in University Students.
H. S. Diehl.

11:00-11:30 Mental Hygiene in University Students.
E. M. deBarry.

11:30-12:00 Infant and Maternal Hygiene
E. C. Hartley.

D Wednesday, February 12, 1930

VETERINARY BUILDING, UNIVERSITY FARM, ST. PAUL
Room 107, First Floor
(Capacity—125)

9:30- 9:30 Discussion and Demonstration of Sources of Infection Through Meats.
The Staff.
(The material for this demonstration and that of the entirely new display tomorrow is made available through the cooperation of Dr. G. E. Totten. Federal Inspector in Charge, U. S. Department of Agriculture, Bureau of Animal Industry, South St. Paul.)

9:30-10:00 a. Mechanism of Milk Secretion.
b. Demonstration of Symptoms of Hypocalcemia.
W. E. Peterson and W. L. Boyd.

10:00-10:30 a. Life Cycle of the Ascarid.
b. Diagnosis of Pullorum Disease: Demonstration of Life Cycle.
H. C. H. Kernkamp.

10:30-11:00 Animal Parasites of Man: Demonstrations.
W. A. Riley.

11:00-11:30 Leukemia in the Fowl: Demonstration.
R. Fenstermacher.

11:30-12:00 Normal Variations in the Calcium and Phosphorus Content of the Blood: Illustrated.
L. S. Palmer.

D Thursday, February 13, 1930

VETERINARY BUILDING, UNIVERSITY FARM, ST. PAUL
Room 107, First Floor
(Capacity—125)

(On display in Room 103, by Veterinary Department, is a Demonstration of Pathological Specimens obtained in Meat Inspection: Relation to Human Health.)

9:00- 9:30 Acidosis in Animals. (Demonstration.)
W. L. Nilson and W. L. Boyd.

9:30-10:00 Relation between Animal and Plant Diseases. (Demonstration.)
E. C. Stakman.
10:00-10:30 Infectious Abortion and Undulant Fever. (Demonstration.)
C. P. Fitch, C. R. Donham and A. L. Delez.
10:30-11:00 Phosphorus Deficiency. (Demonstration.)
C. H. Eckles.
11:00-11:30 The Corpus Luteum, the Oestrus Cycle, and the Treatment of Sterility in the Bovine.
W. L. Boyd.
11:30-12:00 Evaluation of Dietary Materials. (Illustrated.)
Alice Biester.

E Tuesday, February 11, 1930

HENNEPIN COUNTY MEDICAL SOCIETY ROOMS

20th Floor, Medical Arts Building

(Ninth Street South between Nicollet and Marquette Avenues.)
(Capacity—350)

9:00- 9:30 Diabetic Coma.
Donald McCarthy.
9:30-10:00 Medical Clinic.
F. J. Hirschboeck, Duluth.
10:00-10:45 Medical Clinic.
J. S. McLester, Birmingham.
10:45-11:30 Physiology of Liver.
F. C. Mann, Rochester, Minn.
11:30-12:00 Riedel's Struma followed by Myxedema.
Charles N. Hensel, St. Paul.

E Wednesday, February 12, 1930

HENNEPIN COUNTY MEDICAL SOCIETY ROOMS

20th Floor, Medical Arts Building

(Ninth Street South between Nicollet and Marquette Avenues.)
(Capacity—350)

9:00- 9:30 Toxic Myocardium.
Morris Nathanson.
9:30-10:00 Hypothyroidism.
F. H. K. Schaaf.
10:00-10:45 Medical Clinic.
J. H. Means, Boston.
10:45-11:15 Broncho-Oesophageal Fistula; Diehl's Crisis.
Moses Barron.
11:15-12:00 Moving Pictures; Results of Sympathectomy in Chronic Arthritis.
L. G. Rowntree, Rochester, Minn.

E Thursday, February 13, 1930

HENNEPIN COUNTY MEDICAL SOCIETY ROOMS
20th Floor, Medical Arts Building
(Ninth Street South between Nicollet and Marquette Avenues.)
(Capacity—350)

9:00- 9:30 Bronchial Asthma.
A. E. Cardle.
9:30-10:00 Addison's Disease.
Reuben Johnson.
10:00-11:00 Sensory Disturbances; Their Recognition and Significance.
Walter Freeman, Washington, D. C.
11:00-11:30 Clinic in Hematology, Atypical Lymphoid Reactions; Blood Platelet Dyscrasias.
Edgar T. Hermann, St. Paul.
11:30-12:00 Amyloid Disease.
Harry Oerting, St. Paul.

E Friday, February 14, 1930

HENNEPIN COUNTY MEDICAL SOCIETY ROOMS
20th Floor, Medical Arts Building
(Ninth Street South between Nicollet and Marquette Avenues.)
(Capacity—350)

9:00- 9:30 Surgical Treatment of Diabetes.
Macnider Wetherby.
9:30-10:00 Evulsion of Phrenic Nerve in Tuberculosis.
E. K. Geer, St. Paul.
10:00-11:00 Chronic Sinus Infection in Relation to Systemic Disease.
Noble Wiley Jones and F. B. Kistner, Portland, Ore.
11:30-11:30 Arterial Hypertension.
J. A. Lepak, St. Paul.
11:30-12:00 Hypothyroidism.
Charles N. Hensel, St. Paul.

F Tuesday, February 11, 1930

MINNEAPOLIS GENERAL HOSPITAL
(Fifth Street between Sixth and Seventh Avenues)
Sun Porch, First Floor
(Capacity—125)

9:00- 9:45 Clinic on Leukemia.
Moses Barron.
9:45-10:30 Neurological Diagnosis.
Lewis J. Pollock, Chicago.
10:30-11:00 Clinic on Hypothyroidism.
F. H. K. Schaaf.
11:00-12:00 Clinic on Gastro-Intestinal Disease.
E. L. Gardner.

F

Wednesday, February 12, 1930

MINNEAPOLIS GENERAL HOSPITAL
(Fifth Street between Sixth and Seventh Avenues)
Sun Porch, First Floor
(Capacity—125)

9:00-10:00 Clinic on Neurosyphilis.
J. C. Michael.
10:00-11:00 Chest Clinic.
T. A. Peppard.
11:00-12:00 Clinic on Anemia.
J. Davis.

F

Thursday, February 13, 1930

MINNEAPOLIS GENERAL HOSPITAL
(Fifth Street between Sixth and Seventh Avenues)
Sun Porch, First Floor
(Capacity—125)

9:00-10:0 Clinic on Leukemia.
Moses Barron.
10:00-11:00 Clinic on Ramisectomy.
A. A. Zierold.
11:00-12:00 Clinic: Heart Disease in Pregnancy.
M. Nathanson.

F

Friday, February 14, 1930

MINNEAPOLIS GENERAL HOSPITAL
(Fifth Street between Sixth and Seventh Avenues)
Sun Porch, First Floor
(Capacity—125)

9:00-10:00 Clinic on Toxic Myocardium.
M. Nathanson.
10:00-11:00 Clinic on Gastro-Intestinal Diseases.
E. L. Gardner.
11:00-12:00 Clinic on Syphilis and Skin Diseases.
S. Sweitzer.

G

Tuesday, February 11, 1930

MINNEAPOLIS GENERAL HOSPITAL
(Fifth Street, between Sixth and Seventh Avenues)
Clinic Room, Basement Floor
(Capacity—70)

9:00-10:00 Erysipelas Treatment. Comparative Study of more Recent Methods.
W. Ude.
10:00-10:30 Clinical Pathological Conference on Rheumatic Fever Pneumonia.
N. Lufkin and A. Kerkhof.
10:30-12:00 Clinic on Varicose Ulcers with Demonstration of Pathology.
H. O. McPheeters and N. Lufkin.

G Wednesday, February 12, 1930

MINNEAPOLIS GENERAL HOSPITAL
(Fifth Street, between Sixth and Seventh Avenues)
Clinic Room, Basement Floor
(Capacity—70)

9:00-10:00 Crystallization of Our Knowledge of Childhood Tuberculosis.
J. A. Myers.
10:00-11:00 Clinical Pathological Conference on Hodgkin's Disease with Pel Ebstein Fever.
J. Davis and N. Lufkin.
11:00-12:00 Clinical Pathological Conference on Kidney Disease.
E. T. Bell and G. E. Fahr.

G Thursday, February 13, 1930

MINNEAPOLIS GENERAL HOSPITAL
(Fifth Street, between Sixth and Seventh Avenues)
Clinic Room, Basement Floor
(Capacity—70)

9:00- 9:30 X-ray Diagnosis of Tuberculosis of Chest.
W. Ude.
9:30-10:00 Surgical Treatment of Ulcerative Colitis.
O. J. Campbell.
10:00-11:30 Clinic on Varicose Ulcers with Demonstration of Pathology.
H. O. McPheeters and Dr. Lufkin.
11:30-12:00 Conservative Treatment of Diabetic Gangrene.
E. Regnier.

G Friday, February 14, 1930

MINNEAPOLIS GENERAL HOSPITAL
(Fifth Street, between Sixth and Seventh Avenues)
Clinic Room, Basement Floor
(Capacity—70)

9:00-10:00 X-ray Methods in Heart Diagnosis.
W. Ude.
10:00-11:00 Clinical Pathological Conference on Miliary Tuberculosis following Renal Tuberculosis.
J. C. Davis and N. Lufkin.
11:00-12:00 Clinical Pathological Conference on Renal Disease.
E. T. Bell and G. E. Fahr.

H Tuesday, February 11, 1930

ST. MARY'S HOSPITAL
(2500 South Sixth Street)
Assembly Room
(Capacity—400)

9:00- 9:30 Pediatric Clinic.
E. S. Platou.
9:30-10:30 Types of Gastro-Intestinal Neuroses.
Walter C. Alvarez, Rochester, Minn.

10:30-11:30 Clinic on Diseases of Respiratory Tract.
Frederick T. Lord, Boston.
11:30-12:00 Coronary Arterial Disease.
M. H. Nathanson.

H Wednesday, February 12, 1930

ST. MARY'S HOSPITAL
Assembly Room
(Capacity—400)

9:00- 9:30 Cancer of the Stomach; Syphilis of the Stomach.
9:30-10:00 Ophthalmoscopic Examination in General Medicine.
Walter Fink.
10:00-11:00 Diseases of the Colon.
J. A. Bargen, Rochester, Minn.
11:00-11:30 Subarachnoid Hemorrhage of Undetermined Origin.
A. S. Hamilton.
11:30-12:00 Thrombangeitis Obliterans.
H. T. Evans.

H Thursday, February 13, 1930

ST. MARY'S HOSPITAL
(2500 South Sixth Street)
Assembly Room
(Capacity—400)

9:00- 9:30 Exophthalmic Goiter with Exceptional Heart Findings; Report of Case.
Stanley Maxeiner.
9:30-10:00 Present-Day Management of Hyperthyroidism.
Leo Murphy.
10:00-11:00 Essential Hypertension.
W. B. Breed, Boston.
11:00-11:30 Differential Diagnosis in the Upper Urinary Tract.
T. H. Sweetser.
11:30-12:00 Study of Differential Diagnosis of Head Pains; Presentation of Cases.
C. D. Wright.

H Friday, February 14, 1930

ST. MARY'S HOSPITAL
(2500 South Sixth Street)
Assembly Room
(Capacity—400)

9:00- 9:30 Diabetes.
Donald McCarthy.
9:30-10:00 Appendicitis in Early Pregnancy.
10:00-11:00 Undulant Fever and Tularemia.
Walter M. Simpson, Dayton, Ohio.
11:00-11:30 Reactive Depression.
J. C. Michael.
11:30-12:00 Obscure Back Cases.
M. O. Henry.

I

Tuesday, February 11, 1930

SWEDISH HOSPITAL, NEW BUILDING
(Eighth Street at Ninth Avenue South)
Clinical Laboratories, Third Floor
(Capacity—100)

9:00- 9:30 Review of 200 Cases of Functional Gall Bladder Study.
G. T. Nordin.
9:30-10:00 Childhood Tuberculosis.
C. A. Stewart.
10:00-10:30 Cancer Therapy with Special Reference to Metastases.
Charles R. Drake.
10:30-11:00 Sequelae of Head Injuries.
Julius Johnson.
11:00-11:30 Myasthenia Gravis with Dilatation of Duodenum.
A. S. Hamilton.
11:30-12:00 Duodenal Stasis and Obstruction.
C. B. Wright.

J

Wednesday, February 12, 1930

ABBOTT HOSPITAL
(1717 First Avenue South)
(Capacity—60)

9:00- 9:15 Presentation of Cases (Lantern).
F. C. Rodda.
9:15- 9:30 Aspiration Method for Treatment of Laryngeal Diphtheria.
E. S. Platou.
9:30-10:00 Presentation of Cases.
F. W. Schlutz.
10:00-10:15 Presentation of Cases.
E. R. Robb.
10:15-10:30 Presentation of Cases.
Rood Taylor.
10:30-10:45 Presentation of Cases.
N. O. Pearce.
10:45-11:00 Intraperitoneal Transfusion.
David Siperstein.
11:00-12:00 Tuberculosis and Bronchiectasis. Laryngeal Cases.
Chester A. Stewart.

J

Thursday, February 13, 1930

ABBOTT HOSPITAL
(1717 First Avenue South)
(Capacity—60)

9:00- 9:15 Presentation of Cases.
E. J. Huenekens.
9:15- 9:30 Presentation of Cases.
Cecile Moriarty.
9:30- 9:45 Pseudo-Muscular Dystrophy.
Edward Dyer Anderson.

9:45-10:00 Functional Disturbances of Pre-School Child.
Grete Seham.
10:00-10:30 Functional Disturbances of School Child.
Max Seham.
10:30-11:00 Skin Diseases (Lantern Slides).
Henry Michelson.
11:00-12:00 X-ray Studies of Children.
R. G. Allison.

J Friday, February 14, 1930

SWEDISH HOSPITAL, NEW BUILDING
(Eighth Street at Ninth Avenue South)
Clinical Laboratories, Third Floor
(Capacity—100)

9:00- 9:30 Radiation Therapy of Cancer of Prostate.
G. T. Nordin.
9:30-10:00 Bronchiectasis.
C. A. Stewart.
10:00-11:00 Medical Clinic.
C. Saul Danzer, Brooklyn.
11:00-11:30 Medical Cases Illustrating the Method of Defense of the Body.
S. P. Rees.
11:30-12:00 New Methods of Study of Gastric Secretion, Especially with Histamin and Alcohol.
C. B. Wright.

K Tuesday, February 11, 1930

NORTHWESTERN HOSPITAL
(Chicago Avenue and Twenty-Seventh Street)
First Floor
(Capacity—100)

9:00- 9:30 Hearing in Relation to Medicine.
H. Newhart.
9:30-10:00 X-ray in Medicine.
R. G. Allison.
10:00-10:45 Arthritis.
L. G. Rowntree, Rochester, Minn.
10:45-11:30 The Non-Tuberculous Chest.
T. A. Peppard.
11:30-12:00 Pulmonary Tuberculosis.
Everett K. Geer, St. Paul.

K Wednesday, February 12, 1930

NORTHWESTERN HOSPITAL
(Chicago Avenue and Twenty-Seventh Street)
First Floor
(Capacity—100)

9:00- 9:30 Vascular Surgery.
A. A. Zierold.

9:30-10:00 Diabetes.
Franklin Adams, Rochester, Minn.
10:00-11:00 Diabetes.
E. P. Joslin, Boston.
11:00-12:00 Diabetes.
R. M. Wilder, Chicago.

K Friday, February 14, 1930

NORTHWESTERN HOSPITAL
(Chicago Avenue and Twenty-Seventh Street)
First Floor
(Capacity—100)

9:00- 9:30 Carbon Dioxide-Oxygen Studies in Anesthesia.
A. T. Mann.
9:30-10:00 Vincent's Infection from the Dental Standpoint.
Benjamin Sandy.
10:00-11:00 Vincent's Infection.
R. I. Rizer.
11:00-11:30 Tuberculosis of the Rectum.
W. A. Fansler.
11:30-12:00 Thoracic Surgery in Tuberculosis.
A. A. Law.

L Tuesday, February 11, 1930

GLEN LAKE SANATORIUM
(Twelve miles from the Auditorium. Take Excelsior Blvd.)
Assembly Room
(Capacity—500)

9:00- 9:30 Childhood Tuberculosis.
P. M. Mattill.
9:30-10:00 Diagnosis of Tuberculosis.
Francis M. Pottenger, Monrovia, Calif.
10:00-10:30 Collapse Therapy in Pulmonary Tuberculosis.
T. J. Kinsella.
10:30-11:00 X-ray in Diagnosis and Treatment of Pulmonary Tuberculosis.
Malcolm Hanson, Minneapolis.
11:00-11:30 Heliotherapy in Pulmonary and Extra-Pulmonary Tuberculosis.
C. W. Mills, Tucson.
11:30-12:00 Intestinal Tuberculosis.
V. K. Funk.

L Wednesday, February 12, 1930

GLEN LAKE SANATORIUM
(Twelve miles from the Auditorium. Take Excelsior Blvd.)
Assembly Room
(Capacity—500)

9:00- 9:30 General Management of Pulmonary Tuberculosis.
E. S. Mariette.
9:30-10:00 Genito-Urinary Tuberculosis.
Gilbert J. Thomas, Minneapolis.

10:00-10:30 Diagnosis of Childhood Tuberculosis.
Gerald B. Webb, Colorado Springs.
10:30-11:00 Heliotherapy in the Treatment of Tuberculosis.
C. K. Petter.
11:00-11:30 Pathogenesis of the Tubercle.
H. E. Robertson, Rochester, Minn.
11:30-12:00 Pregnancy and Tuberculosis.
F. L. Jennings.

Thursday, February 13, 1930

GLEN LAKE SANATORIUM
(Twelve miles from the Auditorium. Take Excelsior Blvd.)
Assembly Room
(Capacity—500)

9:00- 9:30 General Management of Pulmonary Tuberculosis.
E. S. Mariette.
9:30-10:00 Pneumothorax Studies in Tuberculosis.
James Burns Amberson, Loomis, N. Y.
10:00-10:30 Orthopedic Surgery in Tuberculosis.
E. P. K. Fenger.
10:30-11:00 Effect of Upper Respiratory Infection on Tuberculosis.
S. Cohen.
11:00-11:30 Selection of Cases for Cauterization of Adhesions.
Ralph C. Matson, Portland, Ore.
11:30-12:00 Thoracoplasty.
T. J. Kinsella.

Friday, February 14, 1930

GLEN LAKE SANATORIUM
(Twelve miles from the Auditorium. Take Excelsior Blvd.)
Assembly Room
(Capacity—500)

9:00- 9:30 Extra-Pulmonary Tuberculosis.
E. P. K. Fenger.
9:30-10:00 Thoracoplasty.
John Alexander, Ann Arbor.
10:00-10:30 Intestinal Tuberculosis.
V. K. Funk.
10:30-11:00 Relation of Proctology to Tuberculosis.
W. A. Fansler, Minneapolis.
11:00-11:30 Childhood Tuberculosis.
Philip King Brown, San Francisco.
11:30-12:00 Pregnancy and Tuberculosis.
F. L. Jennings.

Special Features

GLEN LAKE SANATORIUM

Hennepin County supports a sanatorium for tuberculosis which has become one of the outstanding institutions of its kind in the country.

The regular staff of the sanatorium has been supplemented by a large consulting staff of physicians and surgeons in Minneapolis who visit the institution at short and regular intervals and concern themselves particularly with the problems presented in special fields, both in tuberculosis and in the general fields involved in any institution with 700 beds.

The four days of clinics at this institution will exemplify the excellent work done there and will be attractive to the internist, as well as to those interested in this particular field.

A number of the outstanding clinicians of the country will be guests of the staff there and will present special clinics during the morning sessions.

SYMPOSIUM ON THE BIOLOGY OF CANCER

This symposium will take place on the afternoon of Thursday, February 13, and is of interest to every physician because of the fundamental nature of the consideration given. In outlining the symposium, the committee has secured the services of speakers who are the outstanding authorities in each instance.

The discussion centers around the fundamentals of the subject and does not attempt to go into the technic of the management of the diseases grouped under this heading.

SYMPOSIUM ON THE ROLE OF SURGERY IN PULMONARY TUBERCULOSIS

The success which has attended the management of pulmonary tuberculosis is one of the outstanding achievements of our time. The greatest success has been in the prevention of the transmission of the disease and in the cure of the case in which the lesions are early and destruction has not as yet become extensive.

Within the past decade surgery has performed an increasing service for the individual with the more advanced and intractable lesions, and the committee felt that this was a favorable time and place for a study of the rôle which surgery may perform in this disease.

As is the case with the symposium on "The Biology of Cancer," the participation of the outstanding men in this field in the country was sought, and without exception, the invitations given have been accepted. This symposium is the most authoritative presentation of this subject that can be secured in this country today.

PROGRAM FOR THE LADIES IN CONNECTION WITH THE 1930 MEETING OF THE AMERICAN COLLEGE OF PHYSICIANS

Every effort is being made on the part of the women in Minneapolis who are planning the entertainment for the women guests of the American College of Physicians at its annual convention in Minneapolis in February, 1930, to make the time spent in Minnesota both pleasant and profitable.

Since Minneapolis is one of the greatest grain centers of the world, we are happy to accept the invitation of the Washburn-Crosby Flour Mills to visit the Mill and have lunch there as their guests on Tuesday morning, the first convention day. The Washburn-Crosby Company will send cars for the women at the Auditorium at 12:00 o'clock noon, and will return them to their hotels by 2:00 p. m.

That same afternoon the women of the local committee hope to meet in person all of the women guests at a gallery talk and tour followed by a tea at the Minneapolis Institute of Arts, which we feel sure will be of great interest, even to those coming from larger art centers in the East, West or South.

For Tuesday evening, a block of seats has been reserved at the Metropolitan Theatre, where the recent New York success, "Street Scene," will be shown. Opportunity will be given during Monday and Tuesday to procure tickets at the Convention Headquarters. Thus guests may plan to go in pairs or groups and will be sure of sitting together in one section.

We would like to mention in passing, that every night during the week the Bainbridge Players at the Shubert Theatre will put on a play for our special benefit, the title of which will be announced later. We suggest that those who arrive Monday may like to attend the Shubert Theatre Monday evening as no other special plan has been made for that night.

Wednesday noon, the women are invited to attend a luncheon given in their honor at the new Women's Club on Oak Grove Street. In beauty and completeness, the building and its appointments are second to none in this country and we will allow ample time for its inspection and appreciation.

Following the luncheon and tour, the group has been invited to attend a specially arranged exhibit of etchings, prints and Waldorf toys in the galleries of Dr. Mabel Ulrich's Book Shop at Nicollet Avenue and Twelfth Street. This is one of the unique book and print shops of the Northwest.

In the evening of Wednesday, all of the women guests are invited to attend the Convocation and Smoker, and for details of this we ask you to examine the men's program.

Thursday morning at ten o'clock special busses will take the women from the Auditorium through St. Paul's residential section to the Minnesota Historical Society Building, adjoining the State Capitol. A committee of St. Paul women will act as hostesses for a short inspection tour of great interest. Following this, the ladies will be returned to Minneapolis in ample time for lunch and rest before a delightful musicale and tea, arranged by the Hennepin County Medical Society Auxiliary and given in the new rooms of the Hennepin County Medical Society.

Thursday evening will be reserved for the Banquet and Dance at the Curtis Hotel. Once more we urge the ladies to examine the men's program for details of this event.

No definite program has been made on Friday, but on that day, as all through the week, there will be some one at the Information Desk near the Registration Bureau in the Auditorium, ready to give information as to places to lunch, shop or to see a good movie, or to serve in any other way that may be desired.

The Women's Committee in Minneapolis is hoping for a large attendance and is looking forward with great pleasure to making many friends among its guests.

THE UNIVERSITY FARM, CLINICS AND DEMONSTRATIONS

Minnesota is an agricultural state. The University Department of Agriculture and Home Economics, with the Division of Veterinary Medicine, occupies an eminent position on account of its outstanding scientific work. This is promptly translated into practical terms for the use of the people of the state whose livelihood and well-being depend upon the raising of grain and livestock, or the production and sale of commodities related to that fundamental pursuit.

Much of the work in pathology, parasitology, bacteriology, biochemistry, nutrition and endocrinology has a direct bearing on the practice of medicine and offers similar problems. The clinical judgment of Dr. C. P. Fitch, Chief of the Veterinary Division, has enabled him to choose the subjects and speakers that will best bring out the parallel problems and the coinciding points.

The local committee takes pride in offering two morning programs filled with illustrated talks and demonstrations by experts from the various divisions of this typically Minnesota institution. The detailed program is given elsewhere.

The University Farm is in the outskirts of St. Paul. Transportation has been provided by means of special busses which will leave the Nicollet Hotel at 7:45 a. m. Wednesday and Thursday, stopping for pas-

sengers at the Radisson, Dyckman, Curtis and Leamington Hotels. The round trip fare is fifty cents. Taxicab fare is $1.30 per cab, which can accommodate five persons. The time is about twenty-five minutes.

SPECIAL CLINICS AND DEMONSTRATIONS AT THE UNIVERSITY FARM

Minnesota is an agricultural state. Its life depends largely upon the growing of grain and the raising of livestock. The Department of Agriculture and Home Economics is exceptionally important at the State University and includes an outstanding Division of Veterinary Medicine.

The Chief of this division, Dr. C. P. Fitch, with an unusual sense of both clinical and scientific values, has arranged a program of exceptional interest, choosing the experts in pathology, biochemistry, parasitology, nutrition and endocrinology from the entire College of Agriculture and Home Economics.

The opportunities for animal experimentation are unbounded in such an institution. Many of its problems exactly parallel those of clinical medicine. The subjects and speakers for these morning sessions of clinics and demonstrations have been chosen because of their direct bearing on the practice of medicine.

What has the work on animals taught that can be applied to the human patient? Both the practical and the academic phases have been given full attention and the short and well-pointed talks are all accompanied by illustrations or demonstrations.

What do you know about the chemistry of milk production? Would you be interested in seeing a large mammary gland through which is pumped by motor different solutions and from which is obtained milk of all colors and consistencies?

What do you know about the life-cycle of animal parasites? Would you care to see it demonstrated in all its phases, under circumstances where observation is accurate and infallible?

Did you know that acidosis occurs in animals, and that hypocalcemia gives a clear-cut clinical picture? What are the normal variations in the calcium and phosphorus content of the blood and what are the signs of phosphorus deficiency? These conditions have been produced and studied in large mammals, with metabolic processes similar to those of the human patient, by biochemists, nutritional experts and clinical veterinarians, who are reporting an epitome of their findings.

Can you recognize a case of undulant fever? Do you know how this disease is related to infectious abortion in dairy herds which veterinarians have been studying extensively for years before clinicians in general realized that undulant fever was a disease entity?

What is the present status of knowledge in regard to the relation of the corpus luteum to the oestrus cycle? This is to be discussed from the standpoint of sterility and its treatment in the bovine.

The local committee takes pride in offering these two unusual and stimulating programs to The College on Wednesday and Thursday mornings. The seating capacity is limited to 125. Special busses to the University Farm, where these programs are given, will leave the Nicollet Hotel at 7:45 a. m., stopping for passengers at the Radisson, Dyckman, Curtis and Leamington Hotels.

Praxagoras, of Cos, about three hundred years B. C., first recognized that pulsation occurred only in the arteries, although he believed that the pulsation was due to an aeriform fluid, a sort of pneuma.

Antonio Scarpa, born in Friuli in 1747, was the first to regard arteriosclerosis as a lesion involving the inner coats of the arteries. The century and a half elapsing since Scarpa began to write has shown progress in our knowledge of the arteries exceeding many fold that of the twenty-one centuries separating him from Praxagoras.

It would seem that we ought to know now all there is to know about the arteries and their diseases, but new methods and their diseases, but new methods and new points of view have greatly increased our knowledge in recent decades. While vascular disease is not covered in our program

in symposium form, a group of seven papers, each by a master in his field, has been brought together and will be read on Tuesday afternoon.

The Annual Banquet of The College will be held at 7:00 o'clock Thursday evening, February 13, at the Curtis Hotel. All physicians of the Twin Cities and vicinity and visitors attending the session are invited, with their ladies, by the members of The College and its officers to attend this Banquet. Music will be furnished and an address delivered.

Following the Banquet the dance will occur and all are invited to remain.

Tickets for the Banquet, including the dance, are $5.00 per person and these must be purchased at the Information Bureau before 10:00 o'clock Thursday morning.

CONVOCATION OF THE COLLEGE

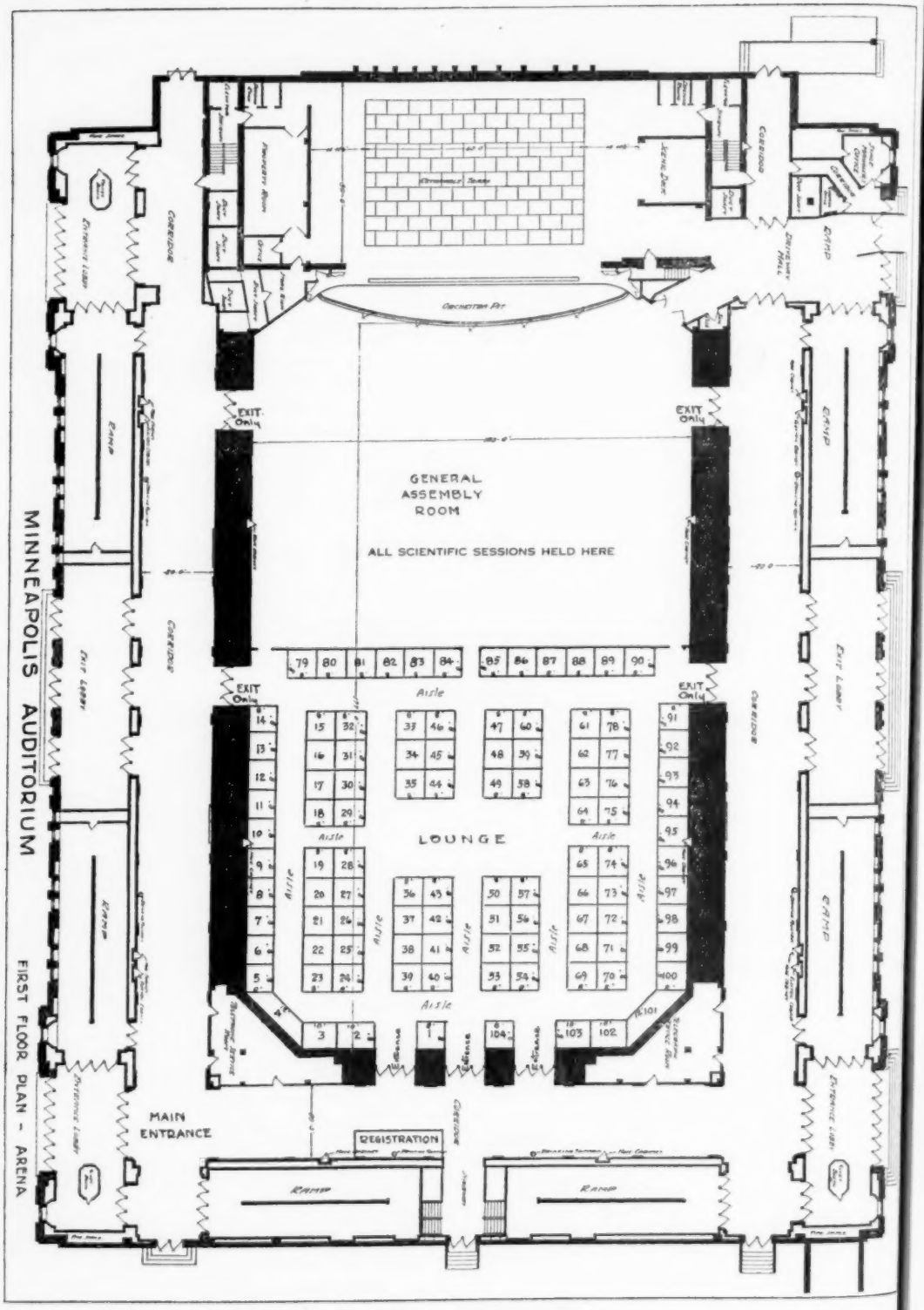
8:00 o'clock Wednesday Evening, February 12, in The Auditorium.

All Fellows of The College and those to be received in Fellowship should be present. Newly elected Fellows who have not yet been received in Fellowship are requested to occupy the central section of seats especially reserved for them.

The Convocation is open to physicians generally and to such of the general public as may be interested.

Following the Convocation Ceremony, the President, Dr. John H. Musser, Jr., of New Orleans, will deliver the annual address to the Masters, Fellows and Associates of The College.

The Smoker will follow the Convocation after a short intermission. An attractive program has been arranged. All physicians with their ladies and friends are invited.



PLAN OF MINNEAPOLIS AUDITORIUM

showing layout of meeting hall, exhibits, registration, etc. The Exhibit and Exposition of medical appliances and apparatus, books, pharmaceutical products, special foods, etc. will be a special feature of the Clinical Session, February 10-14, 1930.

EXPOSITION AND EXHIBITS

The plan of the Minneapolis Auditorium and the arrangement of the exhibits printed on the preceding page show the unusually fine arrangements that have been made for the Minnneapolis Clinical Session. The exhibits will be highly diversified in their variety, and will bring to the attendants at the Clinical Session, the latest and most improved equipment, the best pharmaceutical products, almost the whole library of medical publications, and many other products of especial interest to the internist, pediatrician, neurologist, psychiatrist, radiologist and research worker.

This Exhibit will surpass in size, diversity and popularity any yet conducted by the College. In the midst of exhibits will be located a large and attractive lounge, or lobby, where the attending physicians may rest, visit and hobnob together. There will be comfortable chairs and davenports, writing desks, a public stenographer and other conveniences in the Lounge for the doctors. Besides, the College will have its own booth here where information will be given, the daily bulletin announced, the daily registration and directory posted, and the publications and activities of the College displayed.

The Joseph T. Griffin Decorating Company of Louisville, Ky., who installs the exhibits for the American Medical Association, the Southern Medical Association, the American Hospital Association and other prominent societies, will be in charge of the installation of booths and decoration.

Space	Exhibitor	Address
3	Abbott Laboratories	North Chicago, Ill.
81 & 82	American X-Ray Corporation	Chicago, Ill.
39	Anderson Company, C. F.	Minneapolis, Minn.
34	Battle Creek Food Company	Battle Creek, Mich.
4	Blakiston's Son & Co., P.	Philadelphia, Pa.
30 & 31	Borden Sales Company	New York, N. Y.
59	Boulitte & Company, G.	New York, N. Y.
70	Britesun, Inc.	Chicago, Ill.
74	Brown & Day, Inc.	St. Paul, Minn.
84	Cambridge Instrument Co.	New York, N. Y.
2	Cameron's Surgical Specialty Co.	Chicago, Ill.
51	Carnrick Company, G. W.	Newark, N. J.
103	Chippewa Springs Corporation	Minneapolis, Minn.
9	Dahl Company, Joseph E.	Minneapolis, Minn.
33	Davies, Rose & Co., Ltd.	Boston, Mass.
53	Davis Company, F. A.	Philadelphia, Pa.
42	Davis Sales Company, R. B.	Hoboken, N. J.
32	Dimond-Union Stamp Works	Boston, Mass.
18	Doak Company, Inc., J.	Cleveland, Ohio
86	Gerber Products Division	Fremont, Mich.
102	Gradwohl Laboratories	St. Louis, Mo.
35 & 44	Hoeber, Inc., Paul B.	New York, N. Y.
55	Horlick's Malted Milk Corporation	Racine, Wis.
46	Kalak Water Co.	New York, N. Y.
85	Kellogg Company	Battle Creek, Mich.
87	Laboratory Products Company	Cleveland, Ohio
57	LaMotte Chemical Products Company	Baltimore, Md.
50	Lea & Febiger	Philadelphia, Pa.
69	Lederle Antitoxin Laboratories	New York, N. Y.
101	Lippincott Co., J. B.	Philadelphia, Pa.

1	Macmillan Company, The	New York, N. Y.
41	Mead Johnson Co.	Evansville, Ind.
26	Medical Case History Bureau	New York, N. Y.
58	Medical Protective Co.	Chicago, Ill.
52	Mellin's Food Company	Boston, Mass.
56 & 66	Merck & Company	Rahway, N. J.
15 & 16	Merrell Co., The William S.	Cincinnati, Ohio
36 & 43	Metz Laboratories, Inc., H. A.	New York, N. Y.
19	Mosby Company, C. V.	St. Louis, Mo.
40	Nelson & Sons, Thomas	New York, N. Y.
47, 48 & 49	Petrolagar Laboratories, Inc.	Chicago, Ill.
37 & 38	Physicians & Hospitals Supply Co.	Minneapolis, Minn.
54	Sanborn Company	Cambridge, Mass.
29	Saunders Company, W. B.	Philadelphia, Pa.
10	Spencer Lens Company	Buffalo, N. Y.
56	Squibb & Sons, E. R.	New York, N. Y.
28	Swan-Myers Company	Indianapolis, Ind.
60	Tailby-Nason Company	Cambridge, Mass.
27	Taylor Instrument Companies	Rochester, N. Y.
45	Upsher Smith, Inc.	Minneapolis, Minn.
61, 62, 63. 64, 75, 76, 77 & 78	Victor X-ray Corporation	Chicago, Ill.
36 & 43	Winthrop Chemical Co., Inc.	New York, N. Y.
24	Wood & Company, William	New York, N. Y.

SIDE LIGHTS ON THE EXHIBITS

C. F. Anderson Co., Inc., of Minneapolis, Minnesota, will occupy spaces 67 and 68 in the exhibition to be held in the Minneapolis Auditorium, February 10 to 14, inclusive.

They invite their friends to view their exhibit, which will be complete and of interest to all members of the American College of Physicians

P. Blakiston's Son & Co., Inc.—Books are the tools of the physicians and every member of the American College of Physicians should allot sufficient time for a careful examination of publishers exhibits. We shall offer this year a number of valuable new monographs. Visit our Booth, No. 4. Name the subjects in which you are particularly interested at present.

The Boulitte Company of New York and Paris, makers of Scientific Instruments since 1875, will exhibit and demonstrate in Booth No. 59, the BOULITTE Electrocardiograph, portable and standard models, Pachon's Oscillometer, several types of blood pressure outfits, as well as a number of physiological instruments.

PHYSIOTHERAPY IS A DEFINITE PART OF MEDICINE.—"It is our most modern Therapeutic Agent, it is an indispensable part of Medical and Surgical practice. It should be used as one of the triad of Medicine, Surgery and Physical Therapy." BRITESUN, Inc., Booth No. 70.

At the exhibit of Brown & Day, Inc., of St. Paul, will be displayed a comprehensive line of instruments of precision and supplies required by the Internist in his daily routine. Also a battery of American Sterilizers, specially built for office and Clinic use.

The Cambridge Instrument Co., Inc., pioneer manufacturers of the Electrocardiograph, will exhibit their latest model Electrocardiographs incorporating a number of recent improvements. Other Physiological Instruments of interest to the medical profession will be shown.

The value of "High Visibility in Diagnosis and Surgery"as applied to all phases of major and minor diagnostic, operative and therapeutic procedure will be fully demonstrated at the clinical exhibitions of

Cameron's Surgical Specialty Company, Chicago, Booth No. 2. The demonstration of Cameron's Cauteries will also be a unique feature of the exhibit.

Space 103—Exhibit of the Chippewa Springs Corporation of Chippewa Falls, Wisconsin, to consist of a hollow pyramid of the bottled Chippewa products—Spring Water, Carbonated Water and Dry Ginger Ale, having flood lights inside the pyramid thrown onto the bottles. This is to be surrounded by a counter over which the Chippewa Natural Spring Water will be served and where chemical tests and other interesting demonstrations will prove the Chippewa slogan, "The Purest and softest Natural Spring Water in the World." This will be a truly beautiful and instructive display.

Joseph E. Dahl, of Minneapolis, Minnesota, showing at Booth No. 9, inaugurated a special all night and holiday service to physicians six years ago which has been used by the majority of them in this vicinity, and at this time can supply any item which is needed by the profession.

The distribution of Invertose for obliteration of varicose veins has been handled by this firm in the United States, and recently they have taken over the sales of McIntosh Electrical equipment for the Minnesota territory.

Physicians interested in the treatment of trigeminal neuralgia should visit Booth No. 33. There, Davies, Rose & Co., Ltd., Boston, Mass., will exhibit a preparation used in the relief of pains affecting the area of the fifth nerve, and which preparation is engaging widespread attention.

Cardiologists, also, will find it profitable to visit this booth, as the firm will present a product of particular interest to them, too.

Visiting physicians and their friends are invited to stop at Booth No. 42, where they may secure full information relative to the nature and amount of the food elements present in Cocomalt—also to judge of its quality and flavor.

The booth will be in charge of Miss Elsie Stark, of the R. B. Davis Company, Hoboken, N. J.

Dimond-Union Stamp Works of Boston will have an interesting exhibit at Booth No. 32 of anatomical chart rubber stamps, which make diagnostic or pathological records accurate, graphic and simple.

DIASPORALS—The progressive physician is particularly interested in Colloidal Therapy. At Booth No. 18, interesting literature on the Therapeutic application of Colloidal preparations in the treatment of Lues, Anemia, chronic Arthritis and Carcinoma should commend itself to the Therapist.

Gerber's Strained Vegetables, consisting of Strained Vegetable Soup, Strained Carrots, Strained Spinach, Strained Peas, Strained Tomatoes, Strained Green Beans and Strained Prunes, all packed in 4½ ounce tins. These products are unseasoned, and in addition to convenience, accuracy, and safety in providing the necessary vegetable supplement to the baby's milk diet, are also useful in a wide variety of special diet cases. See them in Booth No. 86.

THE GRADWOHL SCHOOL OF LABORATORY TECHNIQUE—This exhibit will show methods of teaching laboratory technique, with particular reference to the Schilling method. Thick drops, Giemsa-Stained blood smears, Guttaphots showing various diseases, will be shown.

Paul B. Hoeber, Inc., will show their entire line of medical publications and will exhibit for the first time the following book which should be of special interest to the members of the American College of Physicians: "The Creed of A Biologist" by Aldred Scott Warthin. Dr. Warthin's book on "Old Age," published in 1929, was shown for the first time at the Boston meeting, and created great interest.

Among other books of particular interest to the members of the College will be shown Simpson's "Tularemia," Pardee's "Clinical Aspects of the Electrocardiogram," Alvarez's "Mechanics of the Digestive Tract," Roth's "Cardiac Arrythmias," Heberden's "Introduction to the Study of Physic" (edited by LeRoy Crummer and now for the first time published), and the recently issued "Outline of Preventive Medicine" published under the auspices of the

New York Academy of Medicine. With two booths, this house will this year have ample room for visitors, and it is hoped that no member will overlook Booth Nos. 35 and 44.

Horlick's Malted Milk Corporation will be among the exhibitors at the meeting of the American College of Physicians, and plans unusual activities in the interests of its products, Horlick's the Original Malted Milk, natural and chocolate flavor, powder and tablet form and Horlick's Milk Modifier, a maltose and dextrin product. The Horlick exhibit will occupy Booth No. 55.

Kalak, the strongest non-laxative alkaline water of commerce, will be found at Booth No. 46—and attending physicians are invited to visit the booth and test the palatability of this dependable alkalinizing agent.

Kalak Water is offered for therapeutic use under the guidance of the physician only.

Doctors who are interested in a non-stimulating coffee for use in special diets are invited to visit the Kellogg Company exhibit at the Minneapolis Auditorium. Kaffee Hag Coffee will be demonstrated and served with muffins made from Kellogg's All-Bran.

Kaffee Hag is real coffee from which 97 per cent. of the caffeine and indigestible wax has been removed. Diet literature and pads of Prescribed Diet Lists will be distributed.

WHAT IS S. M. A.?—It is generally accepted by physicians trained in the care and feeding of infants that the next best substitute for breast milk is some modification of cow's milk. However, the degree of modification of cow's milk in the majority of cases determines the probability of success and to that end the Babies' and Children's Hospital of Cleveland have modified cow's milk to a remarkable degree and called that modification S. M. A.

S. M. A. is, therefore, a modification of cow's milk in which the fat, protein, carbohydrate and salt content are adjusted in such a way as to produce a mixture that resembles breast milk in its essential, physical, chemical and metabolic properties.

C. M. A. is produced exclusively by The Laboratory Products Company, and you may obtain full details concerning this product from their representatives in Booth No. 87.

At Booth No. 57, LaMotte Simplified Blood Chemistry Apparatus will be demonstrated and all of the new and improved units will be shown. These include outfits for: Blood Sugar, Urine Sugar, Blood Urea, Blood Chlorides, Blood Cholesterol, Blood Calcium-Phosphorus, Blood Bilirubin, Phenolsulfonphthalein Renal Function Test, Hemoglobin, Blood pH, Urinalysis, Urine pH, Icterus Index, Blood Creatinine, Gastric Acidity, Uric Acid, Blood Bromides and Alveolar Air. It is hoped that all those physicians who are interested in blood chemistry will take an opportunity to visit this exhibit. The booth will be in charge of chemists who will be glad to discuss your problems with you.

Lea & Febiger, at Booth No. 50, will have a number of new books and new editions, and will be glad to show them: Eberts—Surgical Diseases of the Thyroid Gland; Faust's Human Helminthology; Hess—Rickets Including Osteomalacia and Tetany; Gershenfeld's Bacteriology and Sanitary Science; Hill's Manual of Proctology; Jelliffe & White—Diseases of the Nervous System; Joslin's Treatment of Diabetes Mellitus; Joslin's Diabetic Manual; Kuntz on the Autonomic Nervous System; Laboratory Methods of the U. S. Army; Mulliner's Mechano-therapy; Park, Williams & Krumwiede on Pathogenic Microorganisms; Pemberton's Arthritis and Rheumatoid Conditions; Schafer's Essentials of Histology; Smith & Wikoff's Materia Medica; Starling's Principles of Human Physiology; Stone's The New Born Infant; Thomas' Dietary of Health and Disease.

J. B. Lippincott Company are introducing six outstanding authors in their new EVERY DAY PRACTICE SERIES under the Editorship of Dr. Harlow Brooks of New York City. This newest enterprise, along with other new and standard works in late editions, is still being shown in a novel, attractive setting. You will find the Lippincott display quite out of the ordinary, and you are invited to make it a place for meeting your friends.

Whatever your specialty of Internal Medicine, visit the Macmillan Booth No. 1. There you will find monographs dealing with subjects of current medical interest. Eyster's VENOUS PRESSURE, one of Macmillan Medical Monographs; Friedenwald's PATHOLOGY OF THE EYE; Parsonnet and Hyman's APPLIED ELECTROCARDIOGRAPHY; Rolleston's LIFE OF SIR THOMAS CLIFFORD ALLBUTT; the Fourth Edition of McCollum and Simmond's THE NEWER KNOWLEDGE OF NUTRITION; Bucky's GRENZ RAY THERAPY; and THE CAMBRIDGE COMPARATIVE PHYSIOLOGY SERIES are but a few of the important titles on display.

A well balanced food compound which meets the nutritional requirements of infants and in many cases has met the problem presented by milk protein idiosyncrasy, is offered in Mead's newest product—Sobee. This as well as Mead's Viosterol (originally Acterol) and the complete group of the better known Mead Infant Diet Materials will be on display at the Mead Johnson Company exhibit, Booth No. 41.

A Patient's History and Accounting System Endorsed and used by Many of the Foremost Physicians in America—The Medical Case History Bureau of New York City will display and demonstrate what leading physicians consider the most complete and efficient system for every branch of medicine—recording every phase of office and home calls. The only system of its kind—made to suit your most exacting individual requirements, yet low priced.

All members of the American College of Physicians and friends are cordially invited to visit Booth No. 58 of the Medical Protective Company. Mr. A. B. Garber of the Home Office in Chicago and Mr. E. E. Patrick, General Agent of Minnesota, will be delighted to have you call, whether merely to say "hello" and renew old acquaintances or to satisfy yourself on some question of malpractice protection. Consider them at your service and feel free to call upon them for anything which may contribute to making this the most pleasant and successful meeting you have ever attended.

The extraordinary interest in Mellin's Food, as applied to illness of adults, that developed during the last session of the American College of Physicians, offers much encouragement to go into further details in regard to the nutritive value of Mellin's Food and the wide range of usefulness of this product in many conditions where a restricted diet is advisable, and particularly in diseases that constitutes a large part of the work of Gastro-enterologists. The purpose, therefore, of the Mellin's Food Company's exhibit is to offer opportunity for free discussion relative to this subject matter, and physicians are cordially invited to call at Booth No. 52.

Take a little trip to the birch woods of Connecticut, and see how the Wm. S. Merrell Company produce the birch oil from which is made their famous Natural Sodium Salicylate.

The Merrell Company are the only pharmaceutical house in the world who produce a Natural Sodium Salicylate from birch oil produced under their own supervision.

At Booth Nos. 15 and 16, the Merrell Company will show a small reproduction of one of their Connecticut mills.

The Nelson Loose-Leaf Medicine and the Nelson Loose-Leaf Surgery, each complete in seven volumes with separate Index Volume, will be on exhibition at Booth No. 40. These outstanding publications carry with them a semi-annual service consisting of (1) a survey of the medical and surgical literature of all countries, reviewed and annotated by 150 of the foremost physicians and surgeons of America, (2) new and revised articles issued under the direction of the Nelson Advisory Board, (3) a special research service free to all subscribers. To quote the U. S. Naval Medical Bulletin: "The list of contributors is practically an honor roll of the surgeons of today." Other Nelson medical publications will also be on exhibition.

SANBORN ELECTROCARDIOGRAF —For testing at office and hospital, or at

patient's homes; Simplified and accurate—easy for technician or nurse to operate.

SANBORN METABOLISM—For clinical diagnosis—the GRAFIC, for specialist and research—the SANBORN BENEDICT with its electric blower circulation.

At Booth No. 54, see the SANBORN ELECTROCARDIOGRAF, SANBORN GRAFIC and SANBORN BENEDICT and DEMONSTRATIONS.

W. B. Saunders Company will exhibit all of their three hundred or more titles; outstanding among these are Beckman's new work on Treatment, Blumer's Bedside Diagnosis, Christopher's Minor Surgery, Campbell's Orthopedic Surgery, Evart A. Graham's new three volume work on Surgical Diagnosis, Cecil's Medicine, Bethea's Medicine Medical Clinics of North America and the Surgical Clinics of North America, Granger's Physical Therapeutic Technic, Norris and Landis Diagnosis by Chest Diseases.

Booth No. 10—Spencer Lens Company of Buffalo, New York—Exhibit of Microscopes and Accessories, Colorimeters, Refractrometers, Microtomes, Dark Field Illuminators, Lantern Slide, Filmslide, and Opaque Projectors and introducing the SPENCER SYSTEM OF VISUAL EDUCATION. Many other things of interest to the Physician and Clinician will be shown."

A physiologically tested vitamin—containing sugar (Vitavose), irradiated ergosterol (Viosterol) products, and a physiologically tested ovarian hormone product will be among the items of interest at the Squibb Booth, No. 56. A competent staff of representatives will be present to answer inquiries about these, and other new Squibb Products.

Interest in Bacteriophage will undoubtedly draw many physicians to Booth No. 28, where members of the scientific staff of Swan-Myers Company will furnish information and literature on this new development in biological therapy. The Swan-Myers laboratories were the first to be licensed by the United States Government for the manufacture of Bacteriophage, and are, at present, the only laboratories in the country to supply Bacteriophage products commercially.

Swan-Myers will also have interesting displays of Ephedrine Products, including Swan-Myers Inhalant, No. 66; Swan-Myers Pollen Extracts; and Para-Psyllia, Swan-Myers, a new mechanical laxative that combines psyllium seed jelly and mineral oil in a pleasing emulsion.

BIG COD FROM NORWAY—During the fishing season of 1928, a cod of record proportions was taken from the Lofoten waters of Norway for Nason & Co., the Norwegian subsidiary of Tailby-Nason Co. This splendid fish, 4 ft. 11 in. long and weighing 30 kilos, will form an interesting part of the exhibit of Nason's Palatable Cod Liver Oil, "The Better Tasting Kind," produced in Nason's plants in Norway, at Booth No. 60.

An announcement of new developments and apparatus will be made at the Exposition of the American College of Physicians, by the Taylor Instrument Companies, Rochester, New York, at Booth No. 27.

Our representatives who will attend the coming Exposition will be men competent to demonstrate and discuss the technique of operation of our instruments and their value in service.

We will be very glad to have members of the American College of Physicians come to our exhibit and investigate our products without any obligation other than to give us an opportunity to present reasons for development and service value of the instruments.

"The Story of Foxglove Farm," told in three minutes in movie form, is of major interest to physicians. Digitalis is one of the five most important drugs—its potency may be a matter of life or death to the patient. Every physician should know the processes and precautions necessary for the production of potent digitalis. It is a drug he cannot afford to take a chance on. It will be worth while to visit Booth No. 45, where the film will be shown by James Upsher Smith, of the Upsher Smith Company.

The Victor X-Ray Corporation will demonstrate, at Booth Nos. 61, 62, 63, 64, 75, 76, 77, and 78, its Model "A" Shock Proof

X-Ray Unit which, in addition to being 100% electrically safe, presents many original control features, such as calibrated autotransformer control, Victor-Kearsley Stabilizer and voltage compensator, which permit a simplified standardized technic hitherto unattainable. There will also be exhibited a comprehensive collection of radiographs made with this Unit.

William Wood and Company, of New York, now celebrating their 126th year as medical publishers, will welcome old and new friends at Booth No. 24, and exhibit specimen copies of about two hundred of their publications, including many new books and such famous standard works as Bailey—Histology; Bailey and Miller—Embryology; Cabot—Physical Diagnosis; Cunningham—Anatomy; Chapin and Royster—Diseases of Children; Chetwood—Urology; Mathews—Physiological Chemistry; Stedman's Medical Dictionary, and of course the indispensable French—Index of Differential Diagnosis.

Minneapolis As a Medical Center

By S. Marx White, M.D., *Minneapolis, Minnesota*

MINNEAPOLIS as a medical center is among the newer points in the New World. Its attractions are shared with those of its twin city, St. Paul. The population of Minneapolis in 1930 is over 500,000, and together with St. Paul and the immediate suburbs of both, the metropolitan area lays valid claim to nearly a million people.

The first hospital in Minneapolis was founded in 1871, 120 years after the foundation of the Pennsylvania Hospital in Philadelphia in 1751, which lays claim to be the oldest institution of this kind in this country. This was also exactly 100 years after a Royal Charter was granted in 1771 to "The Society of the Hospital in the City of New York in America." This was the second hospital within the present limits of the Union if we except that in Manila, Philippine Islands, acquired by conquest and not a product of our normal national growth.

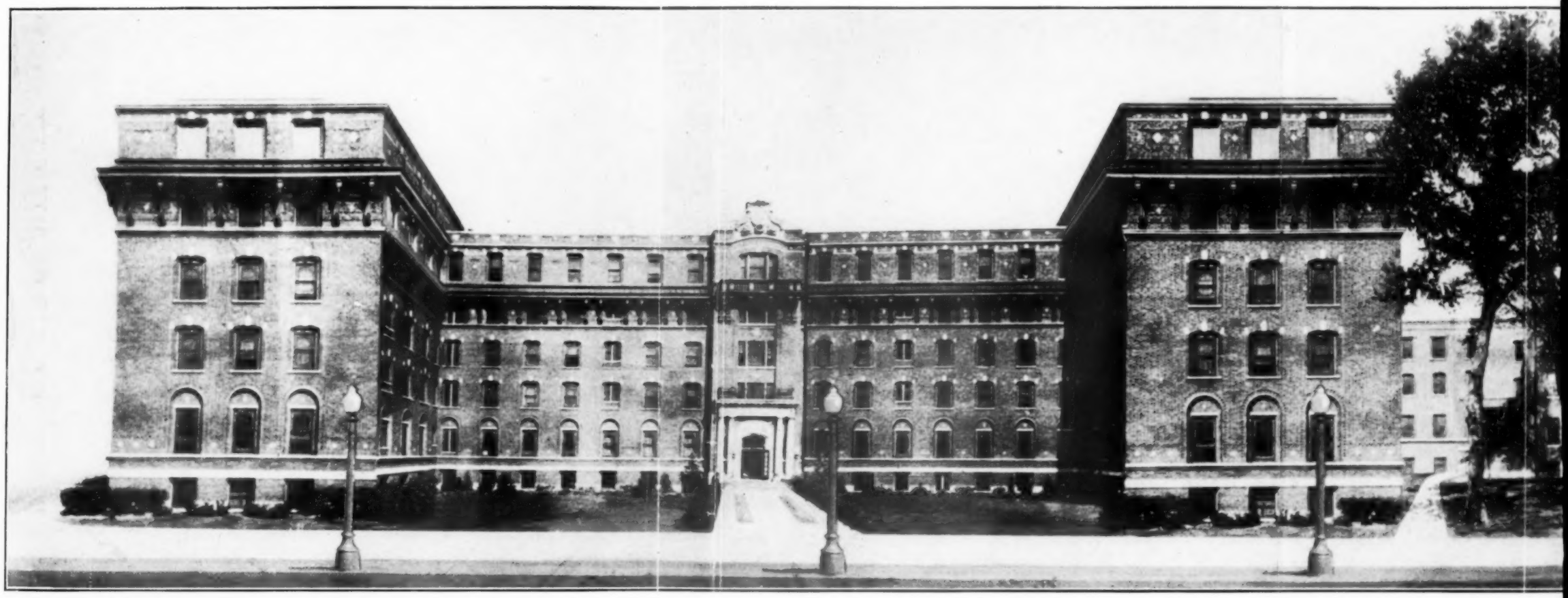
The history of Medicine in Minnesota has been determined by the social conditions and has paralleled the rapid growth. The freedom from tradition and the rise of medical service and medical education in this western metropolis exemplifies the development in the social and economic life.

Dr. Richard Olding Beard, who has done a great service in collecting and recording the facts of this recent history, and to whom the writer hereby acknowledges his debt, shows that following the period of the Preceptor the period of the Private Medical College in Minnesota began parallel with that of the foundation of the first hospital in 1871 in the organization of "The St. Paul Medical School, Preparatory, for Medical Instruction."

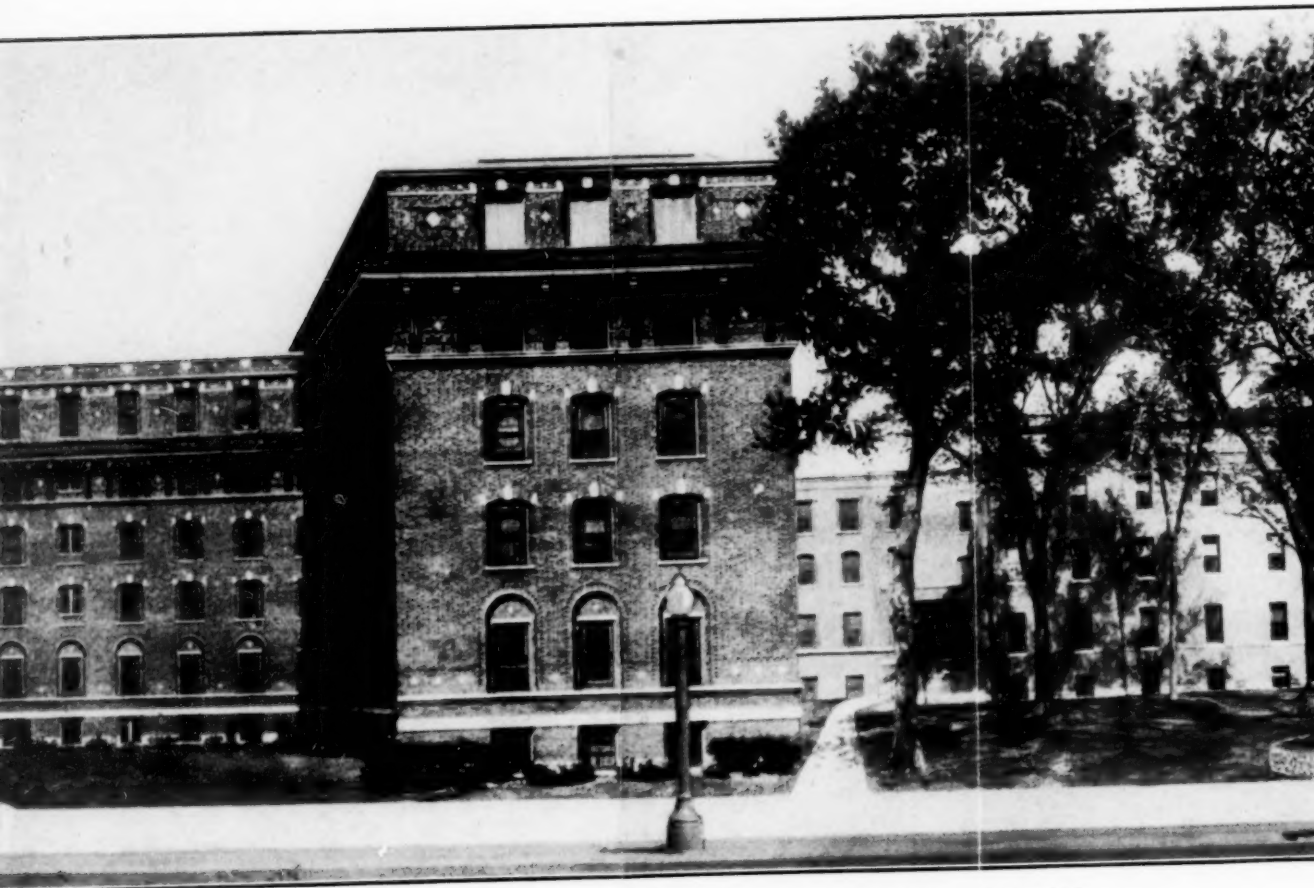
For three years before this, however, students who were "reading medicine" in the doctors' offices in St. Paul had been meeting in a little room perhaps a dozen feet square in the second story of a little stone deadhouse where occasionally an amputated limb was dissected, and they were at odd times met and quizzed by preceptors.

This "Medical School Preparatory" had a corps of 8 teachers, a course of 4 months' study, and was designed to prepare students for a better understanding of the lectures to be heard later in medical college. The arrangement of terms of study was such that "they would not interfere with the winter course of the Chicago Colleges."

Another private school, the Winona Medical School Preparatory, was begun in Winona, Minnesota, in 1872. They neither granted degrees nor conferred diplomas. They had no Alumni.

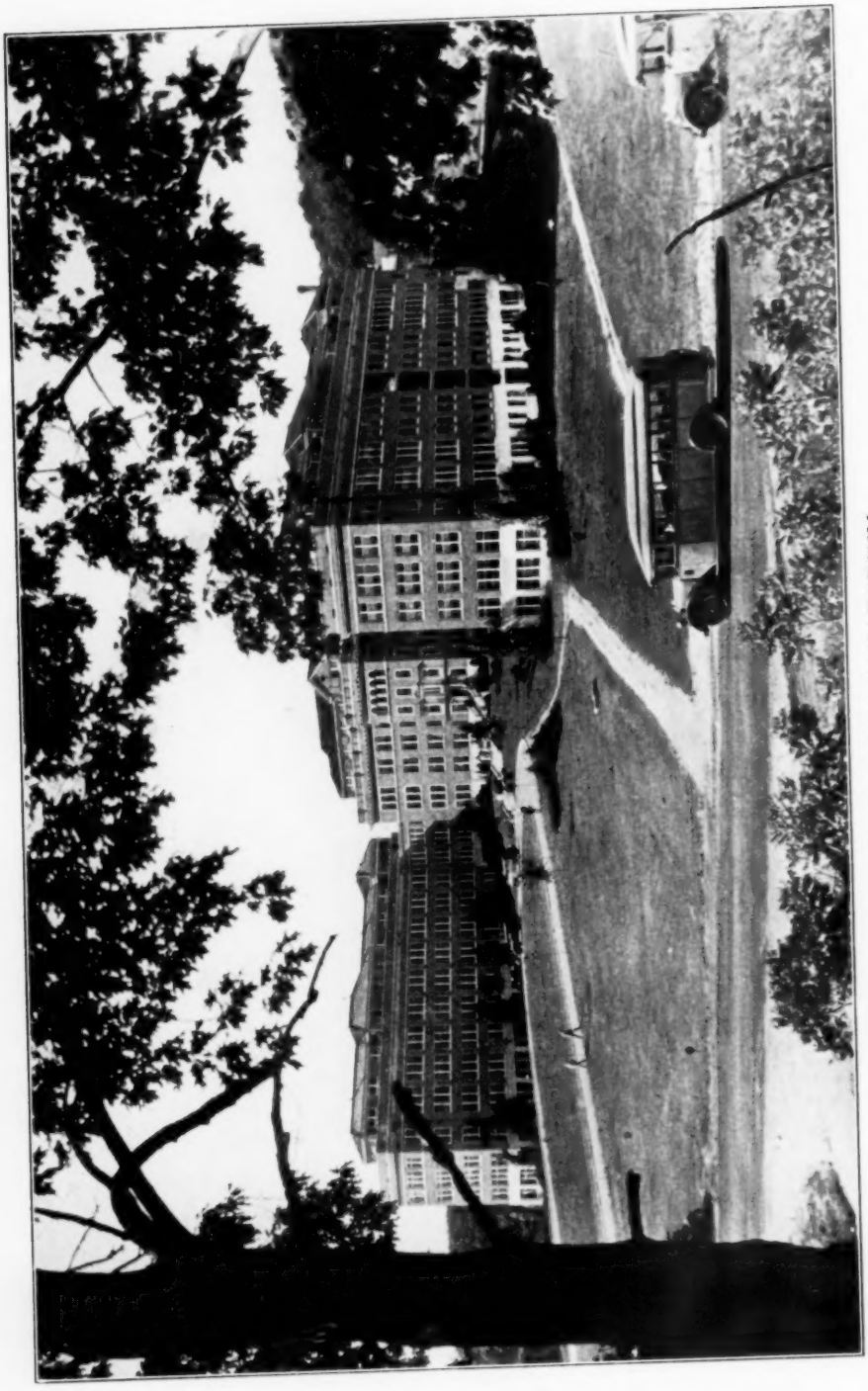


ST. MARYS HOSPI
Minneapolis, Minn



ST. MARYS HOSPITAL
Minneapolis, Minn.

SHRINERS HOSPITAL,
Minneapolis, Minn.



GLEN LAKE SANATORIUM
Minneapolis, Minn.

The St. Paul Medical College was organized as the Medical Department of Hamline University in 1878 and closed with the spring session of 1881. Its Faculty combined with additional physicians of St. Paul and physicians of Minneapolis to found the Minnesota College Hospital in the last named city. It is said that the élite of St. Paul and Minneapolis gathered on the 31st day of October, 1881, in the elegantly fitted lecture room of the College to witness the opening of the school. The first Commencement exercises were held on March 24th, 1882.

In 1883 the University created the Department of Medicine of the University of Minnesota, its Faculty being a non-teaching and purely examining body. This body during a brief period served as an educational influence felt in the medical schools of Minnesota and of other states as evidenced by the qualifications required of candidates for the state examinations and quoted by Dr. Beard as follows:

1. Attendance upon one full course of lectures upon the subject of each study under examination.

2. A familiarity with the literature of the subject.

3. Clinical and laboratory experience.

4. Skill in the actual use of physical and chemical tests in diagnosis, etc.

5. A certificate of dissections of the

NEW ASBURY HOSPITAL
916 E. 15th St.
Minneapolis, Minn.

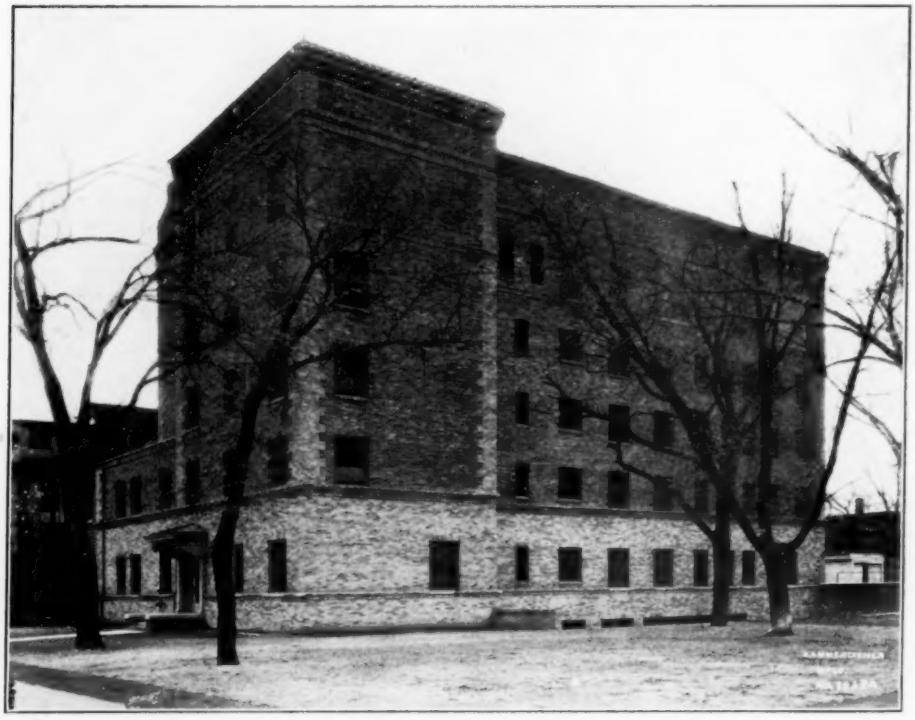
muscular, nervous, and circulatory systems.

In the subjects for examination are named, as prerequisites: in Physiology, the demonstration of normal tissues and products and the relation of the living body to its environments; in Pathology, the demonstration of specimens and examination of cases for diagnosis and the use of chemical agents and the microscope to this end; under Practice, the use of diagnostic instruments and a systematic examination and record of cases.

In 1883 another new college was created under the name of the Minneapolis College of Physicians and Surgeons which, in 1895, was adopted by Hamline University as its Department of Medicine and continued so until its fusion with the Medical School of the University of Minnesota in 1908.

During the earlier years this School granted no degrees, but referred its students to the Department of Medicine of the State University for examination, it being remembered that this Department of Medicine was then purely an examining body.

Meanwhile the Minnesota Hospital continued its courses and during the session of 1884-5 a unique announcement was made by its Dean that "Dr. John F. Fulton, Professor of Opthalmology and Otolaryngology will give a free clinic on diseases of the eye and ear at the College building upon each Friday. All indigent afflicted are in-



ST. ANDREW'S HOSPITAL

vited to avail themselves of the attention now, for the first time in the history of our State, offered to them."

Dr. Fulton is living and active, an honored citizen of St. Paul today.

In 1885 the St. Paul members of the Faculty of the Minnesota College Hospital resigned and the name was changed to the Minnesota Hospital College, moving to a new building in September, 1886. The St. Paul members of the Faculty reorganized the St. Paul Medical College which opened in the fall of 1885 and likewise dedicated a new building in 1886.

In October, 1886, the Minnesota Homeopathic Medical College was organized and lasted for two years with a faculty of 16 and students numbering 20.

In 1887 an independent State Board of Medical Examiners was created by the Legislature. With the single exception of an antiquated measure in South Carolina, this was the first Act of its type upon the statute books of any state and the Act since that day has been the model of most of the Medical Practice Acts in the United States. In the same year the Board of Regents of the University of Minnesota was petitioned to establish a teaching Department of Medicine of high grade in the University, and the Legislature was asked to provide for its maintenance. In February, 1888,

MINNEAPOLIS GENERAL HOSPITAL

the faculties of the Minnesota Hospital College and the St. Paul Medical College offered to surrender to the Board of Regents their charters and tendered their properties for the temporary use of the State, and a month later the Minnesota College of Homeopathic Medicine did likewise.

The proposals were accepted by the Regents and faculties were named and organized for the Colleges of Medicine and Surgery and of Homeopathic Medicine and Surgery. Later, Colleges of Dentistry and Pharmacy were added.

Thus, in October, 1888, the first entrance examinations were held and systematic instruction begun in a course of study covering three years of six months each.

In 1890 the Medical College term was lengthened to eight months.

In 1893 the Legislature provided for the removal of the Department of Medicine to the University Campus and with that Act University instruction in Medicine in Minnesota may be said to have received its greatest impetus.

In 1900-01 entrance examinations to the College of Medicine and Surgery were made identical with those of other departments of the University and some election was provided for in certain special subjects. Beginning with the opening session of 1901, the

ST. BARNABAS HOSPITAL, FOUNDED 1871

college year was extended to nine months.

In the fall of 1903 a six-years' course looking to the degrees of B.S. and M.D. was begun; the first degree to be conferred at the close of the fourth year, and the latter at the end of the sixth year; the last two years of the course for the Bachelor's degree being given in the Medical School. Later the degree of M.B. was given at the completion of the required six years, and the degree M.D. given at the completion of a required year of internship in an approved hospital.

The history of the hospitals of the University of Minnesota begins with the announcement of a bequest from the estate of Dr. and Mrs. A. F. Elliott to be devoted to the building of the Elliott Memorial Hospital. This was promptly followed by provision through a group of philanthropic citizens of Minneapolis for the purchase of a hospital site.

In 1906, Dr. Frank Fairchild Wesbrook, who had come in 1896 as Professor of Patholoy and Bacteriology and was Director of the Laboratories of the State Board of Health, was made Dean of the Medical School and became the moving spirit in a period of unprecedented development in medical education in Minnesota.

In 1906 a plan was adopted by which all medical education in Minne-

NORTHWESTERN HOSPITAL
Minneapolis, Minn.

sota should be unified in the University. The Medical School of Hamline University was discontinued and certain members of that Faculty were invited to positions on the University teaching corps. The School of Homeopathic Medicine and Surgery of the University survived but a little time longer.

The development of the University Hospitals, begun with the Elliott Memorial unit, has been slow but continuous. The Todd Memorial and the Cancer Institute increased greatly the teaching facilities, and the year 1929 has witnessed the completion of the Eustis Memorial and the hospital of the Students' Health Service, together with the transfer of the Out-Patient Department to the University Hospital group of buildings.

To atempt to cover in detail all the progress of the past twenty years would be tiresome and is at this point unnecessary. A great Medical School is in full operation. An important medical center is established and serves a far-flung territory. The cities of Minneapolis and St. Paul, by the keenness of their rivalry, are compelled to an adoption of the most modern facilities. The proximity of the unique and world-famous Clinic and Mayo Foundation at Rochester, less than 100

NEW $700,000 SWEDISH HOSPITAL BLDG.
10th Ave. So. & 8th St.
Minneapolis, Minn.

miles away, provides an additional stimulus.

In addition to under-graduate instruction, an important type of graduate instruction in Medicine has been established, functioning for the Medical School and for the Mayo Foundation, under the Graduate School of the University of Minnesota.

Candidates for the higher degree of M.S. and Ph.D. in the various departments of Medicine, Surgery, and the Medical Sciences take their work either in the Medical School in Minneapolis or at the Mayo Foundation in Rochester.

The pursuit of true graduate study by a rapidly growing number of men and women has had a profound effect upon the character of teaching in the Medical School and has been a large factor in the constantly increasing contributions to knowledge in Medicine.

When Dr. Wesbrook was chosen to head the University of British Columbia in 1913, Elias P. Lyon was chosen his successor as Dean.

The first step by the University providing arrangements by which heads of clinical departments devote their entire time to teaching and investigation was taken in 1915 when Dr. L. G. Rowntree was appointed to head the Department of Medicine. Provision was agreed upon by which a small hospital should be arranged for his private

MATERNITY HOSPITAL, Inc.
2215 Glenwood Ave.
Minneapolis, Minn.

patients in one of the houses on the Campus. The latter part of the arrangement was never carried out but he was given space for an office in one of the buildings of the Medical School and was allowed to see patients there as long as he remained. This arrangement terminated in 1920 with his removal to the Mayo Foundation in Rochester.

In 1918 the late Dr. Julius Parker Sedgwick gave up his private practice in Pediatrics and became a full-time Professor with the privilege of consultation.

With these beginnings the principle of full-time heads of departments and of increasing full-time employment on the part of University clinical teachers has been growing as opportunity was afforded and, with the exception of the Departments of Obstetrics and Gynecology and of Ophthalmology and Otolaryngology, the clinical Departments now have full-time teachers in charge.

The system under which they work is known as the Harvard System and may be characterized as "geographical full-time"; the latter expression meaning that all of the teacher's work is done in one place. He does not maintain an outside office; he is not affiliated with any outside group, nor is he on the active staff of any private hos-

AERIAL VIEW OF UNITED STATES HOSPITAL NO. 106
This Hospital Is Located on the Banks of the Mississippi Just Outside of the West City Limits of Minneapolis and on the Fort Snelling Military Reservaton

pital; his outside work is limited to consultation with other members of the Medical Profession, and in general the full-time members of the Medical School Faculty conform with the regulations for outside work as outlined in the rules and regulations of the University of Minnesota governing all the departments of the institution. This system is virtually that in use at Harvard, Columbia, in partial use at the University of Iowa and in some others.

The hospitals of Minneapolis provide the housing for this most significant type of medical service. The University Hospitals comprise the Elliott Memorial, the Todd Memorial, the Cancer Institute, the Eustis Memorial, and the Hospital for the Students' Health Service, with a total of 480 beds. The buildings house also the Out-patient Department of the Medical School. The Hospital is located on a commanding site overlooking the gorge of the Mississippi and the buildings of the Medical School and of the Departments of Biology of the University are close by.

The Minneapolis General Hospital is a tax-supported institution, receives some partial payment of per diem costs from patients sufficiently able to pay, and has 474 beds, of which 386 are general and 88 in the contagious pavilion. It is located at 5th Street and 7th Avenue South, within nine

THE TOURTELLOTTE MEMORIAL DEACONESS HOME AND THE NEW ASBURY HOSPITAL

blocks of the Auditorium. Connected with it, but in the outskirts of Minneapolis, is the Parkview Sanatorium for chronic patients, with 140 beds. A large voluntary service staff is selected from physicians of the City and University Faculty. One member of the Faculty is on full-time and two on part-time paid service. There are 3 Teaching Fellows, 8 chief Residents, and 24 Interns on the professional house staff.

Of the private and semi-private hospitals, St. Barnabas is the oldest. It was founded in 1871 and was the hospital referred to in the second paragraph of this article. It is situated at 901 South Sixth Street, is a general hospital, and has 170 beds.

Abbott Hospital is located at 1717 First Avenue South, is a general hospital with a large children's pavilion, and has a total of 100 beds.

The New Asbury Hospital is located at 915 East 15th Street, is a general hospital, and has 140 beds.

Eitel Hospital is located at 14th and Willow Streets facing Loring Park, and has 130 beds.

Fairview Hospital, at 2316 Sixth Street South, is a general hospital, with 200 beds.

Hillcrest Surgical Hospital at 501 Franklin Avenue West, has 75 beds.

FAIRVIEW HOSPITAL
Minneapolis, Minn.

The Lutheran Deaconess Hospital, 1412 East 24th Street, is a general hospital, and has 150 beds.

Maternity Hospital, at 2215 Western Avenue, is obstetrical and pediatric, and has 100 beds.

Northwestern Hospital, 2627 Chicago Avenue, covers the fields of medicine, surgery and pediatrics, and has 200 beds.

St. Andrews Hospital, 712 Fifth Street S.E., provides general service, and has 100 beds.

St. Mary's Hospital, 2500 South Sixth Street, is a general hospital, with 250 beds.

The Shriners' Hospital for Crippled Children, one of eleven hospital units distributed throughout the country, is located at 2025 East River Road, and has 62 hospital beds.

The Swedish Hospital at 723 Tenth Avenue South, has just completed and dedicated a new building. It provides general service and has a total capacity at present of 322 beds.

Thomas Hospital is a hospital for tuberculosis, with 65 beds, and is situated at 2340 Sixth Street South.

Glen Lake Sanatorium, which is the sanatorium for tuberculosis for Hennepin County, is in a suburb of Minne-

HILL CREST SURGICAL HOSPITAL
501 West Franklin
PRIVATE GENERAL HOSPITAL
Operated by Drs. Galla, Macnie, Baxter and Hilkutt
Maintains Accredited Nurses Training School of 36 Student Nurses

apolis reached by frequent and rapid bus service, and has more than 700 beds.

United States Veterans Hospital No. 106 is located at Fort Snelling, about 7 miles from the Auditorium, is a general and tuberculosis hospital and has a normal capacity of 469 beds, with a maximum capacity of 541 beds.

The hospitals briefly mentioned here are shown in the photographs accompanying this article.

The total hospital capacity of Minneapolis, when only its active general beds are included is, therefore, 2891. When the United States Veterans Hospital, Glen Lake Sanatorium, with Parkview, Shriners, and Thomas hospitals, i.e., the more chronic and special forms of hospitalization and sanatorium care in and about this medical center, are counted, their beds number 1436; the total of all forms of hospital beds being, therefore, 4327.

The value of any group functioning as a center lies, however, not in the character of the buildings nor in the excellence of the equipment. These are necessary in order that provision be made for modern types of work, and the background of history and the details of physical equipment have been sketched only that an idea may be formed as to the status of economic development.

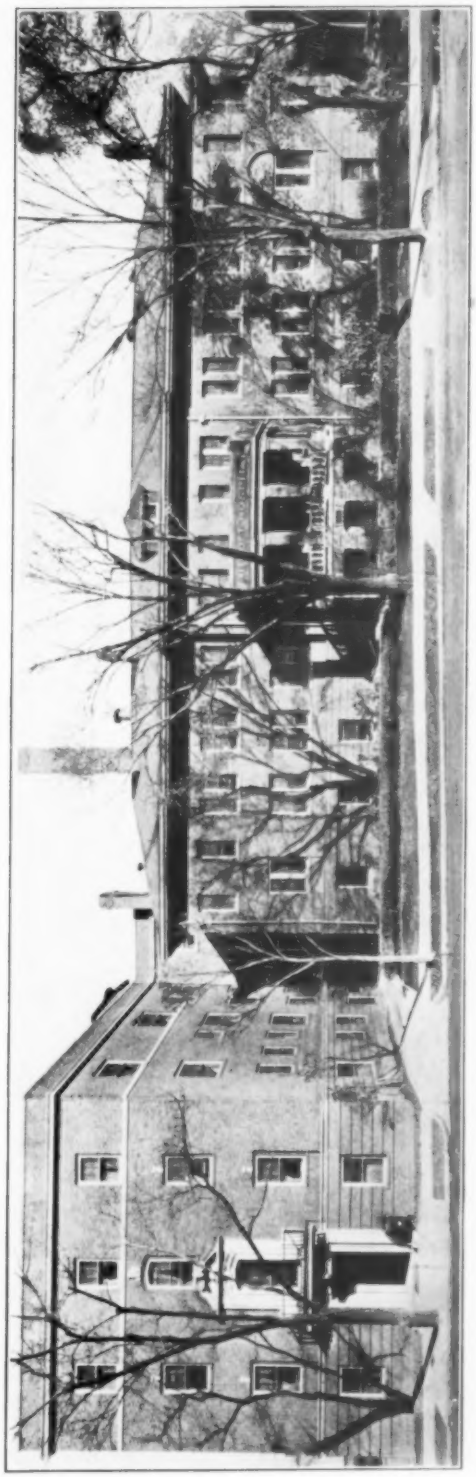
EITEL HOSPITAL
Minneapolis, Minn.

The spirit of the men whose lives have gone into the making can be caught only by long and searching study. There are those whose time, in part at least, is now being given to attempts to put into the record before it is too late something of the lives of these men, the very mention of whose names has been impossible.

Our past is short, but of it we may be justly proud. The great medical centers of Minnesota live in an active present and look forward to a greater future.

LUTHERAN DEACONESS HOSPITAL
1412 E. 24th St.
Minneapolis, Minn.

UNIVERSITY HOSPITAL, UNIVERSITY OF MINNESOTA



ABBOTT HOSPITAL

To Readers of Papers

What arrangements for illustration do you desire for the paper you are to present at the Minneapolis session the week of February 10?

A lantern will be provided for the standard size lantern slides. If x-ray films are to be shown in illuminating box, we should know that and have proper preparation made. If you are to present moving picture films and are bringing your own projection apparatus, we should know that and have provision made for the kind of current you desire. If we will need to provide projection apparatus for moving picture films we must know the size of the films to be shown.

In a word, if apparatus of any kind is needed in the presentation of your paper, we must have before January 15th a full description or statement of all the material to be provided by the local committee. Technical details should be furnished wherever necessary.

Another matter of importance which concerns each essayist relates to newspaper publicity during the meeting. I am aware that most of us desire in every way to avoid any newspaper publicity and will do anything to prevent it. It is just as clear, however, that the meeting of The College is one of importance and the public has a right to know what is going on in our profession.

The Hennepin County Medical Society has a committee on publicity which has been functioning effectively for some time and is co-operating with our committee for this meeting. One of the purposes of the committee is to get before the public in proper form information for those capable of giving it, and the coming meeting will afford an opportunity for the exercise of this function. The committee proposes to see that medical information is given to the press in dignified and proper form, knowing that if this is not done, the press will secure its own information and that the form in which it is published is usually, as we view it, extremely ineffective and does not bring out the greatest values in our work in medicine.

You may feel that your particular paper has no interest for the general public, but it happens that the newspaper and not we will make this decision. In order that the committee may be prepared to aid the press in the proper interpretation and news presentation of the addresses, our committee is asking that you furnish the committee on publicity with an abstract of your paper, or if it is ready by that time, a copy of the manuscript. The purpose of this is that the members of the committee on publicity may be informed in advance and prepared to aid the press in evaluating your material and bringing out of it the greatest values to the public.

The abstract or manuscript should reach us by January 15 at the latest and should be addressed to Dr. J. A. Myers, Chairman, Committee on Publicity, 730 La Salle Building, Minneapolis.